

FIGURE 1

BEST AVAILABLE COPY

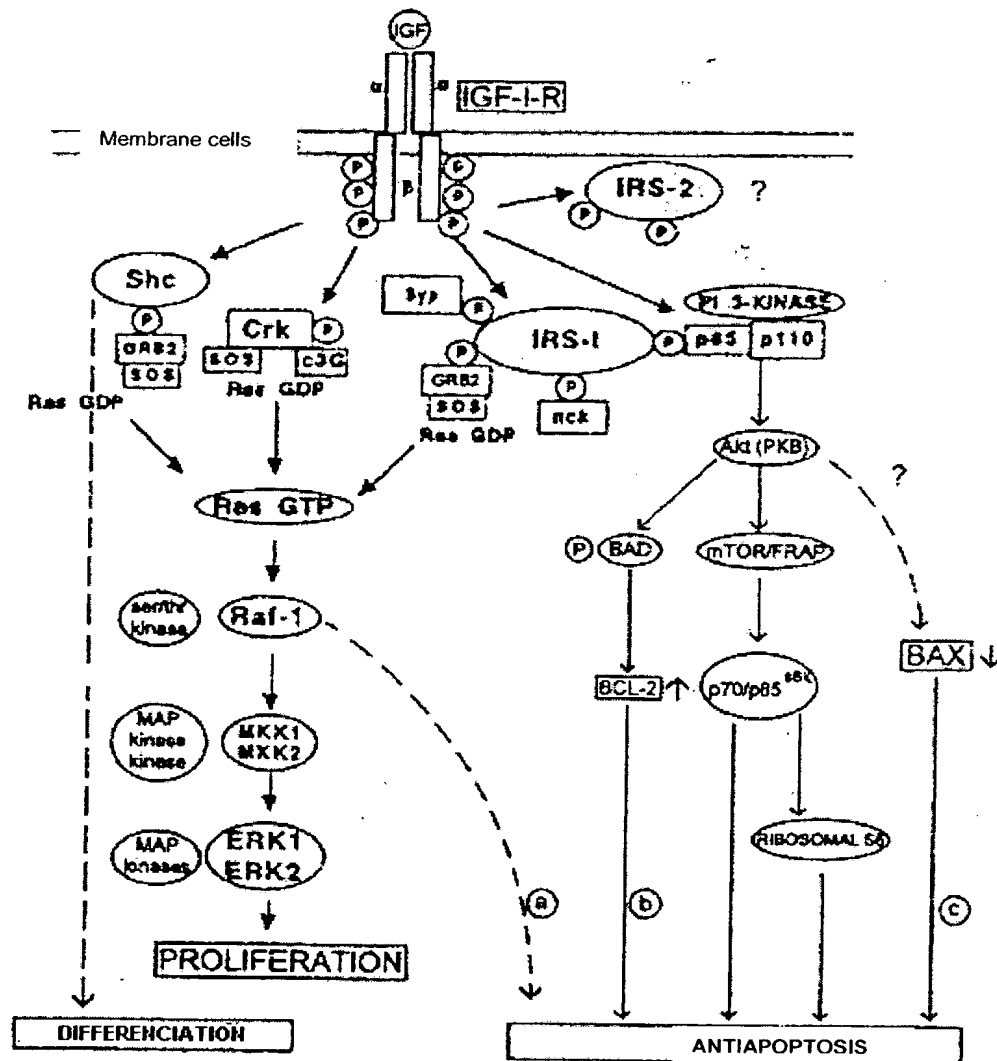


FIGURE 2

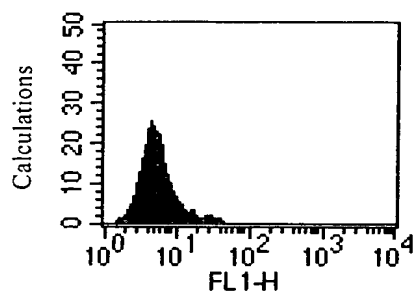


FIGURE 3A

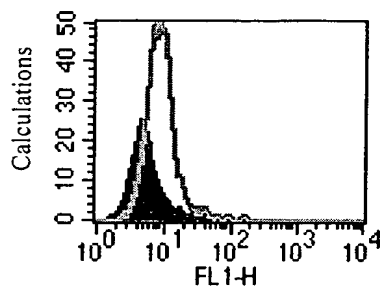


FIGURE 3B

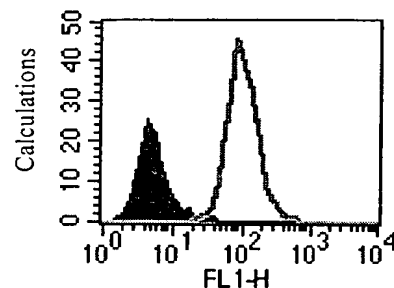
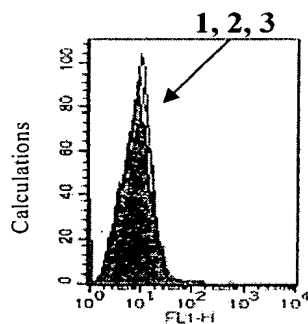
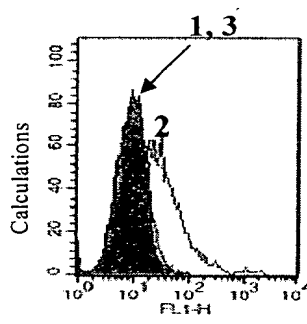


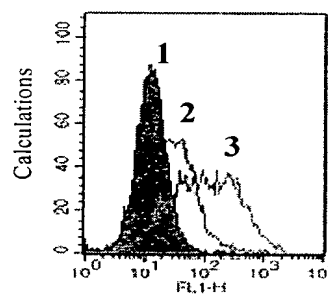
FIGURE 3C



Nontransfected cells



IGF-IR+ cells



IR+ cells

FIGURE 4A

FIGURE 4B

FIGURE 4C

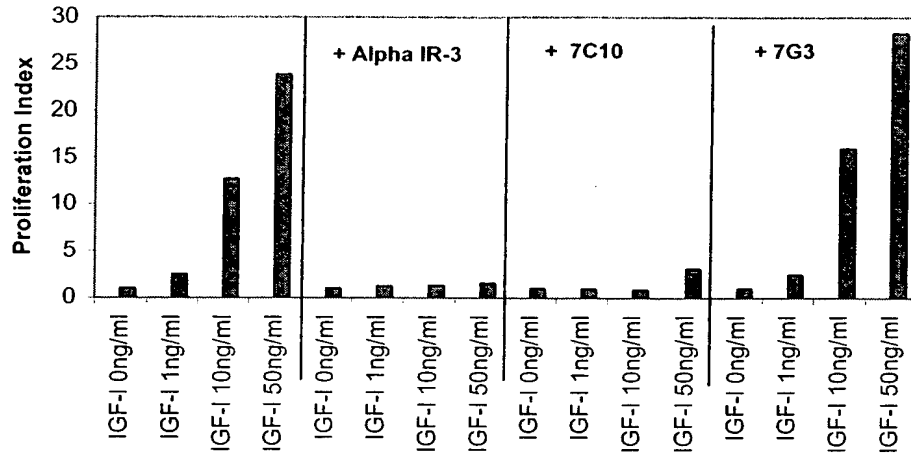


FIGURE 5

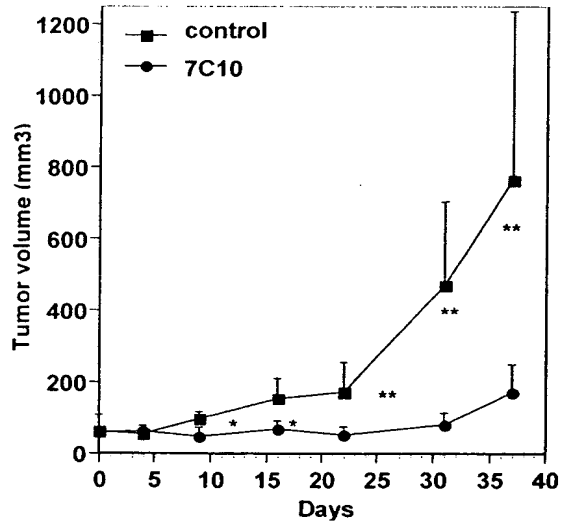


FIGURE 6A

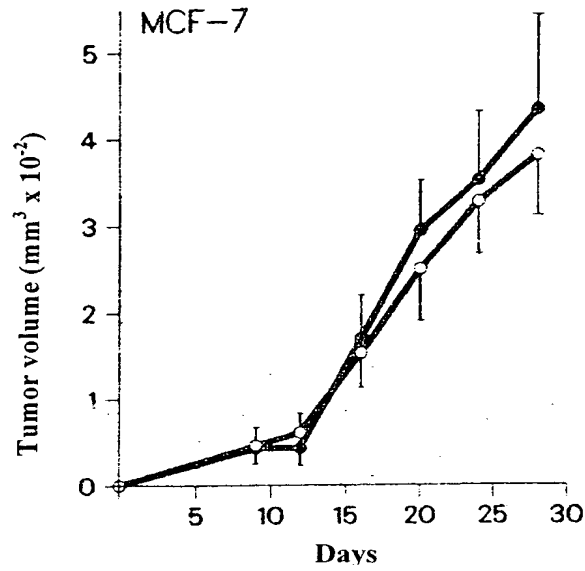


FIGURE 6B

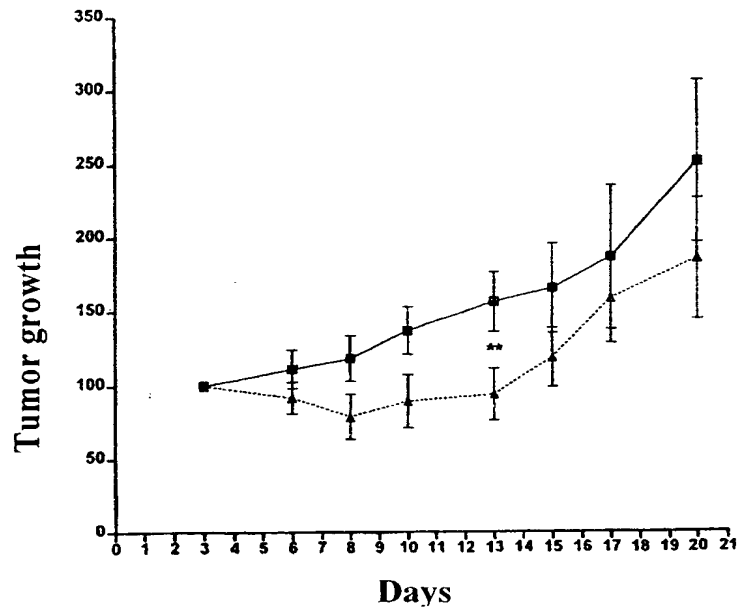


FIGURE 6C

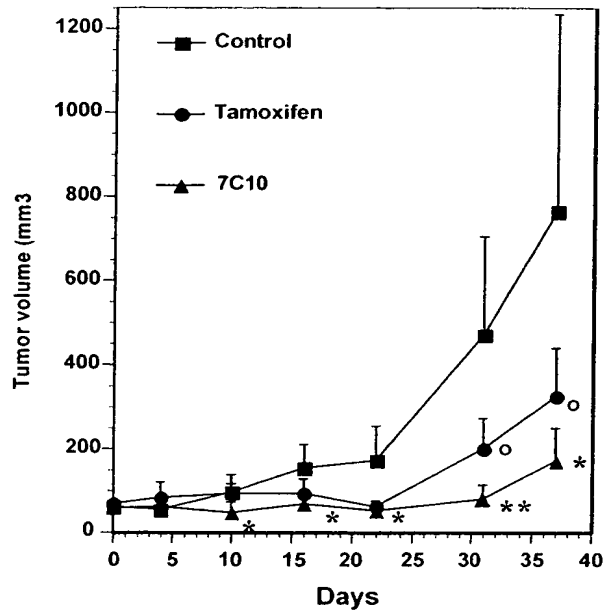


FIGURE 7

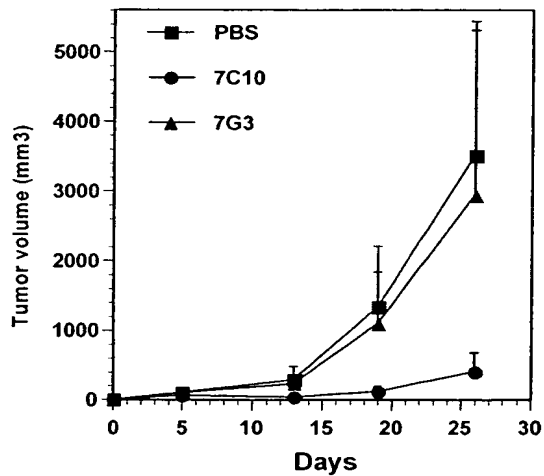


FIGURE 8A

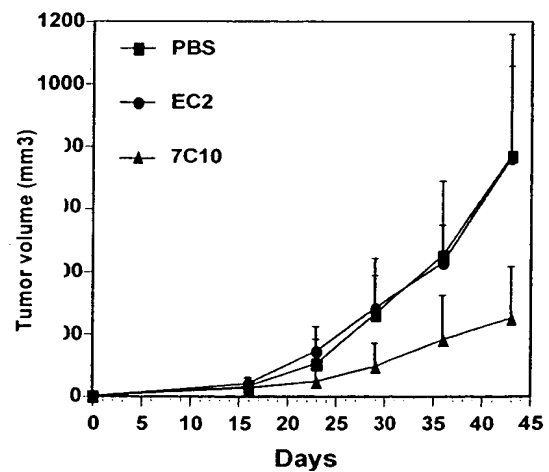


FIGURE 8B

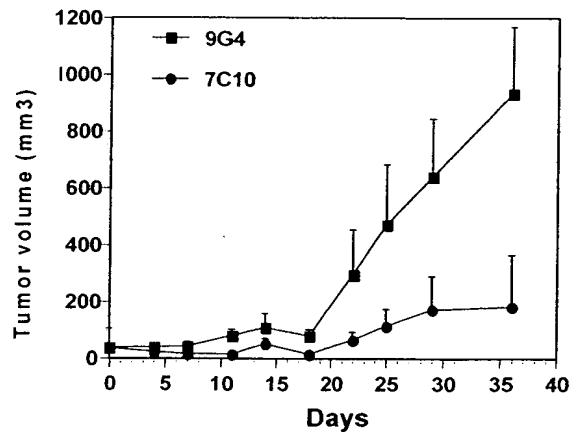


FIGURE 8C

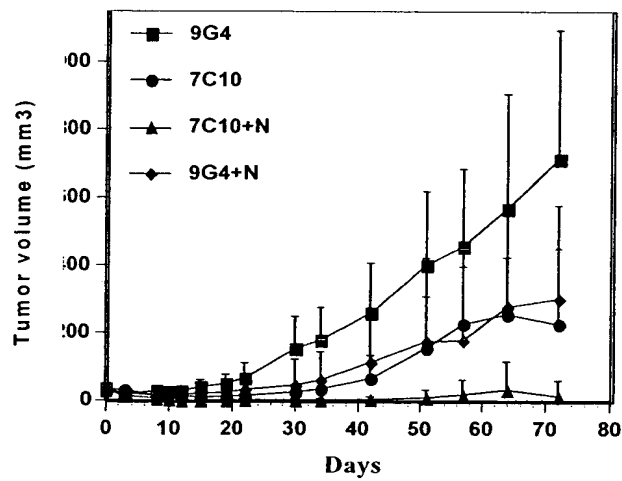


FIGURE 9

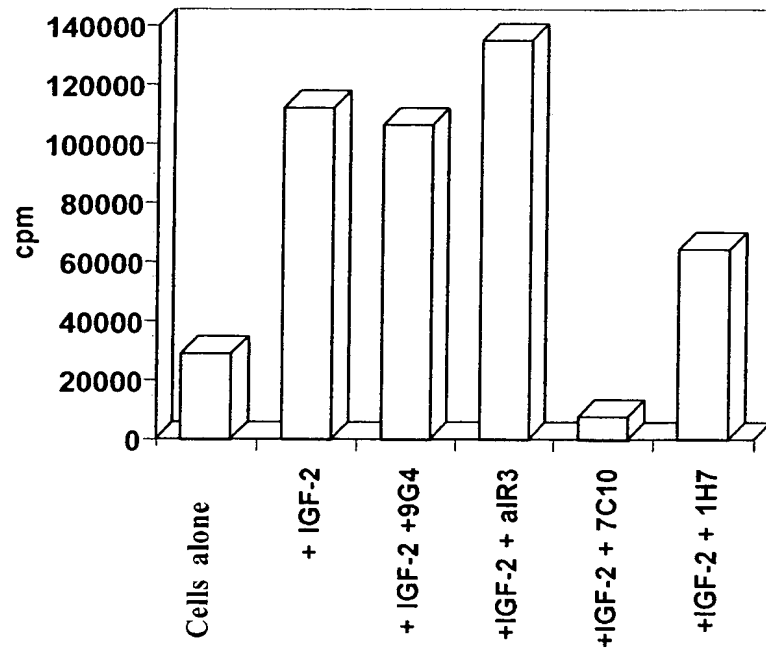


FIGURE 10

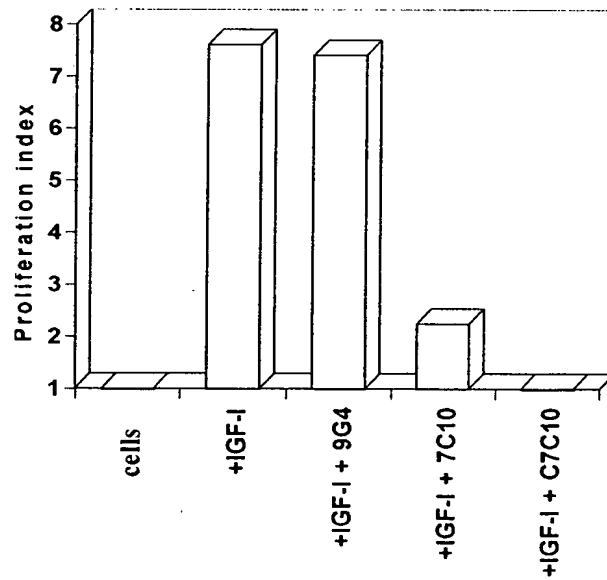


FIGURE 11

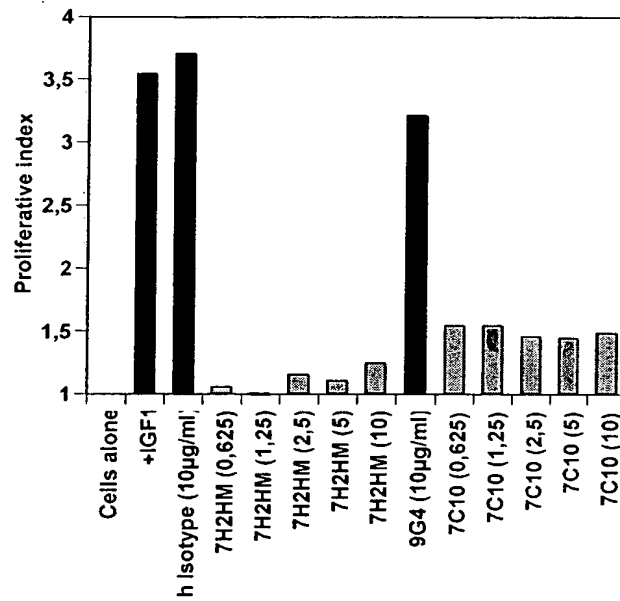


FIGURE 12

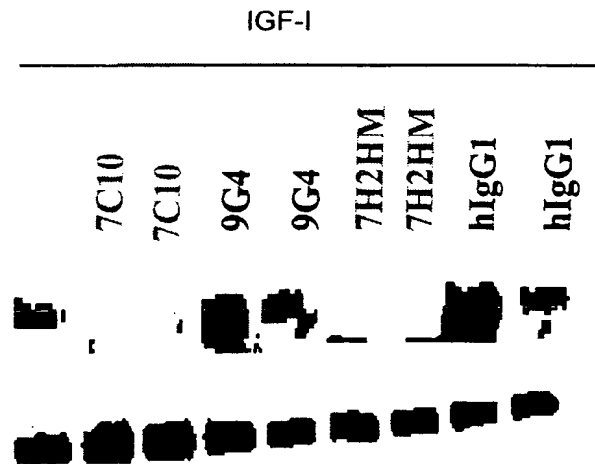


FIGURE 13

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ATGAAGTTGCCTGTTAGGCTGTTGGTGCTGATGTTCTGGATTCTGCTTCCAGAAGTGAT
1  -----+-----+-----+-----+-----+-----+ 60
TACTTCAACGGACAATCCGACAACCACGACTACAAGACCTAAGGACGAAGGTCTTCACTA
ATGAAGTTGCCTGTTAGGCTGTTGGTGCT
      oligo MKV-1          L M F W I P A S R S D -
                          3' end      leader peptide
GTTTTGATGACCCAAATCCCACTCTCCCTGCCTGTCAGTCTTGGAGATCAAGCCTCCATC
61  -----+-----+-----+-----+-----+-----+ 120
CAAACTACTGGGTTTAAGGTGAGAGGGACGGACAGTCAGAACCTCTAGTTCGGAGGTAG

V L M T Q I P L S L P V S L G D Q A S I -

TCTTGCAATCTAGTCAGAGCATTGTACATAGTAATGGAACACCTATTTACAATGGTAC
121 -----+-----+-----+-----+-----+-----+ 180
AGAACGTCTAGATCAGTCTCGTAACATGTATCATTACCTTTGTGGATAAATGTTACCATG

S C R S S Q S I V H S N G N T Y L Q W Y -
                        CDR 1
CTGCAGAAACCAGGTCAGTCTCCAAAGCTCCTGATCTACAAAGTTTCCAACCGACTTTAT
181 -----+-----+-----+-----+-----+-----+ 240
GACGTCTTTGGTCCAGTCAGAGGTTTCGAGGACTAGATGTTTCAAAGGTTGGCTGAAATA

L Q K P G Q S P K L L I Y K V S N R L Y -
                        CDR 2
GGGGTCCCAGACAGGTTCAAGTGGCAGTGGATCAGGGACAGATTTCACTCAAGATCAGC
241 -----+-----+-----+-----+-----+-----+ 300
CCCCAGGGTCTGTCCAAGTCACCGTCACCTAGTCCCTGTCTAAAGTGTGAGTTCTAGTCG

G V P D R F S G S G S G T D F T L K I S -

AGCGTGGAGGCTGAGGATCTGGGAGTTTATTACTGCTTTCAAGGTTACATGTTCCGTGG
301 -----+-----+-----+-----+-----+-----+ 360
TCGCACCTCCGACTCCTAGACCTCAAATAATGACGAAAGTTCCAAGGTACAAGGCACC

S V E A E D L G V Y Y C F Q G S H V P W -
                        CDR 3
GG
ACGTTTCGGTGGAGGCACCAAGCTGGAAATCAAACGGGCTGATGCTGCACCAACTGTATCC
361 -----+-----+-----+-----+-----+-----+ 420
TGCAAGCCACCTCCGTGGTTCGACCTTTAGTTTGCCCGACTACGACGTGGTTGACATAGG

T F G G G T K L E I K

      MKC oligo
TAGAAGGGTGGTAGGTCA
ATCTTCCCACCATCCAGT
421 -----+-----+-----+-----+-----+ 438
TAGAAGGGTGGTAGGTCA
  
```

FIGURE 14

1 ATGATGGTGTAAAGTCTTCTGTACCTCTTGACAGCCATTCTGGTATCCTGTCTGATGTA 60
 -----+-----+-----+-----+-----+-----+
 TACTACCACAATTCAGAAGACATGGACAACCTGTCGGTAAGGACCATAGGACAGACTACAT
 MHV-12 ATGATGGTGTAAAGTCTTCTGTACCT
 MHV-8 ATGAGAGTGTGATTCTTTTGTG
 L L T A I P G I L S D V -
 3' end leader peptide
 CAGCTTCAGGAGTCAGGACCTGGCCTCGTGAAACCTTCTCAGTCTCTGTCTCTCACCTGC
 61 -----+-----+-----+-----+-----+-----+ 120
 GTCGAAGTCTCAGTCCTGGACCGGAGCACTTTGGAAGAGTCAGAGACAGAGAGTGGACG

 Q L Q E S G P G L V K P S Q S L S L T C -

 TCTGTCACCGGCTACTCCATCACCGGTGGTTATTTATGGAACCTGGATCCGGCAGTTTCCA
 121 -----+-----+-----+-----+-----+-----+ 180
 AGACAGTGGCCGATGAGGTAGTGGCCACCAATAAATACCTTGACCTAGGCCGTCAAAGGT

 S V T G Y S I T G G Y L W N W I R Q F P -
 CDR 1
 GGAAACAAACTGGAGTGGATGGGCTACATAAGCTACGACGGTACCAATAACTACAAACCA
 181 -----+-----+-----+-----+-----+-----+ 240
 CCTTTGTTTGACCTCACCTACCCGATGTATTCGATGCTGCCATGGTTATTGATGTTTGGT

 G N K L E W M G Y I S Y D G T N N Y K P -
 CDR 2
 TCTCTCAAAGATCGAATCTCCATCACTCGTGACACATCTAAGAACCAGTTTTTCCTGAAG
 241 -----+-----+-----+-----+-----+-----+ 300
 AGAGAGTTTCTAGCTTAGAGGTAGTGAGCACTGTGTAGATTCTTGGTCAAAAAGGACTTC

S L K D R I S I T R D T S K N Q F F L K -

 TTGAATTCTGTGACTAATGAAGACACAGCTACATATTACTGTGCAAGATACGGTAGGGTC
 301 -----+-----+-----+-----+-----+-----+ 360
 AACTTAAGACACTGATTACTTCTGTGTCGATGTATAATGACACGTTCTATGCCATCCCAG

 L N S V T N E D T A T Y Y C A R Y G R V -
 CDR 3
 GGG
 TTCTTTGACTACTGGGGCCAAGGCACCACTCTCACAGTCTCCTCAGCCAAAACGACACCC
 361 -----+-----+-----+-----+-----+-----+ 420
 AAGAAACTGATGACCCCGGTTCCGTGGTGAGAGTGTGAGGAGTCCGGTTTTGCTGTGGG

F F D Y W G Q G T T L T V S S
 oligo MHC-1
 GGTAGACAGATAGGTGAC
 CCATCTGTCTATCCACTG
 421 -----+-----+-----+-----+-----+ 438
 GGTAGACAGATAGGTGAC

FIGURE 15

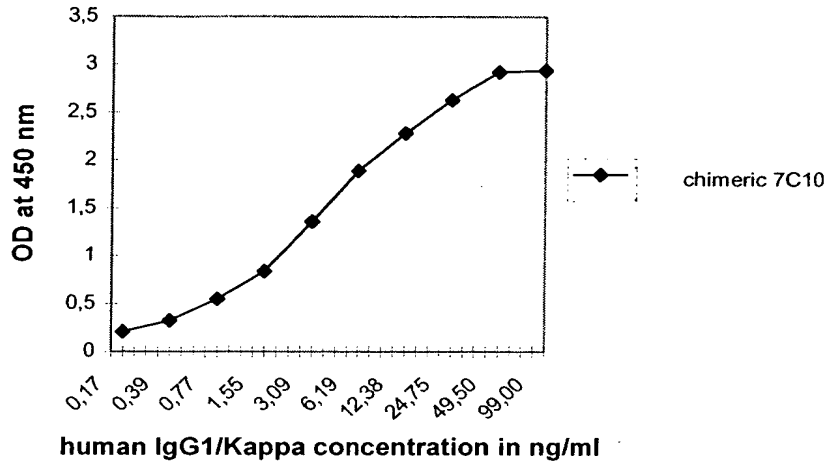


FIGURE 16

	3	7		CDR 1
7C10 VL mouse	DVL	MTQIPLSLPVSLGDQASISC	RSSQSIVHSNGNTYLQ	
DRB1-4.3T.....			E
C94-5B11'CLT.....			E
Kabat sgII mouse	..V...T..	L.....	E

		CDR 2
7C10 VL mouse	WYLQKPGQSPKLLIY	KVSNRLY GVPDRFSGSGSGTDFTL
DRB1-4.3	FS
C94-5B11'CL	FS
Kabat sgII mouse	FS

	77		CDR 3
7C10 VL mouse	KISSVEAEDLGVIYC	FQGSHPWT	FGGGTKLEIK
DRB1-4.3	...R.....	F ..S...D..	
C94-5B11'CL	...R.....		
Kabat sgII mouse	...R.....	T ...Y.	

FIGURE 17

		CDR 1	
7C10 VL mouse	DVLMTQIPLSLPVSLGDQASISC	<u>RSSQSIVHSNGNTYLO</u>	
GM607	.IV...S.....TP.EP.....LL....YN..D	
DPK15/A19	.IV...S.....TP.EP.....LL....YN..D	
Kabat sgII hu	.IV...S.....TP.EP.....LL..D.XX..X	

		CDR 2	
7C10 VL mouse	WYLQKPGQSPKLLIY	<u>KVSNRLY</u>	GVPDRFSGSGSGTDFTLK
GM607Q....	LG...AS
DPK15/A19Q....	LG...AS
Kabat sgII huQ....	L...AS

		CDR 3	
7C10 VL mouse	ISSVEAEDLGVYYC	<u>FQGSHPWT</u>	FGGGTKLEIK
GM607	..R.....V.....	M.ALQT.Q.	..Q...V...
DPK15/A19	..R.....V.....	M.ALQT.	
Kabat sgII hu	..R.....V.....	M.ALQX.R.	..Q...V...

FIGURE 18

		CDR 1	
7C10 VL mouse	DVLMTQIPLSLPVSLGDQASISC	<u>RSSQSIVHSNGNTYLO</u>	
GM 607	.IV...S.....TP.EP.....LL....YN..D	
7C10 VL Humanized 1	..V...S.....TP.EP.....	
7C10 VL Humanized 2	.IV...S.....TP.EP.....	

		CDR 2	
7C10 VL mouse	WYLQKPGQSPKLLIY	<u>KVSNRLY</u>	GVPDRFSGSGSGTDFTL
GM 607Q....	LG...AS
7C10 VL Humanized 1Q....		
7C10 VL Humanized 2Q....		

		CDR 3	
7C10 VL mouse	KISSVEAEDLGVYYC	<u>FQGSHPWT</u>	FGGGTKLEIK
GM 607	...R.....V.....	M.ALQT.Q.	..Q...V...
7C10 VL Humanized 1	...R.....V.....		..Q...V...
7C10 VL Humanized 2	...R.....V.....		..Q...V...

FIGURE 19

MluI
 |
 GTCAGAACGCGTGCCGCCACCATGAAGTTGCCTGTTAGGCTGTTGGTGCTGATGTTCTGG
 1 -----+-----+-----+-----+-----+ 60
 CAGTCTTGCGCACGGCGGTGGTACTTCAACGGACAATCCGACAACCACGACTACAAGACC

M K L P V R L L V L M F W -
 Peptide leader
 TTTCTGCTTCCAGCAGTGATGTTGTGATGACTCAGTCTCCACTCTCCCTGCCCCGTCACC
 61 -----+-----+-----+-----+-----+ 120
 AAAGGACGAAGGTCGTCAC TACAACACTACTGAGTCAGAGGTGAGAGGGACGGGCAGTGG

2
 F P A S S S D V V M T Q S P L S L P V T -
 CCTGGAGAGCCGGCCTCCATCTCCTGCAGGTCTAGTCAGAGCATTGTACATAGTAATGGA
 121 -----+-----+-----+-----+-----+ 180
 GGACCTCTCGGCCGGAGGTAGAGGACGTCCAGATCAGTCTCGTAACATGTATCATTACCT

CDR 1
 P G E P A S I S C R S S Q S I V H S N G -
 KpnI
 |
 AACACCTATTTGCAATGGTACCTGCAGAAGCCAGGGCAGTCTCCACAGCTCCTGATCTAT
 181 -----+-----+-----+-----+-----+ 240
 TTGTGGATAAACGTTACCATGGACGTCTTCGGTCCCGTCAGAGGTGTCGAGGACTAGATA

N T Y L Q W Y L Q K P G Q S P Q L L I Y -
 AAAGTTTCTAATCGGCTTTATGGGGTCCCTGACAGGTTTCAAGTGGCAGTGGATCAGGCACA
 241 -----+-----+-----+-----+-----+ 300
 TTTCAAAGATTAGCCGAAATACCCAGGGACTGTCCAAGTCACCGTCACCTAGTCCGTGT

CDR 2
 K V S N R L Y G V P D R F S G S G S G T -
 GATTTTACACTGAAAATCAGCAGAGTGGAGGCTGAGGATGTTGGGGTTTATTACTGCTTT
 301 -----+-----+-----+-----+-----+ 360
 CTAAAATGTGACTTTTAGTCGTCTCACCTCCGACTCCTACAACCCCAAATAATGACGAAA

D F T L K I S R V E A E D V G V Y Y C F -
 CAAGGTTACATGTTCCGTGGACGTTTCGGCCAAGGGACCAAGGTGGAATCAAACGTGAG
 361 -----+-----+-----+-----+-----+ 420
 GTTCCAAGTGTACAAGGCACCTGCAAGCCGGTTCCTGGTTCCACCTTTAGTTTGCACTC

CDR 3
 Q G S H V P W T F G Q G T K V E I K
 BamHI
 |
 TGGATCCTCTGCG
 421 -----+-----+-----+ 433
 ACCTAGGAGACGC

FIGURE 20

MluI
 |
 GTCAGAACGCGTGCCGCCACCATGAAGTTGCCTGTTAGGCTGTTGGTGCTGATGTTCTGG
 1 -----+-----+-----+-----+-----+ 60
 CAGTCTTGCGCACGGCGGTGGTACTTCAACGGACAATCCGACAACCACGACTACAAGACC

M K L P V R L L V L M F W -
 Leader peptide

TTTCCTGCTTCCAGCAGTGATATTGTGATGACTCAGTCTCCACTCTCCCTGCCCGTCACC
 61 -----+-----+-----+-----+-----+ 120
 AAAGGACGAAGGTCGTCACTACAACACTACTGAGTCAGAGGTGAGAGGGACGGGCAGTGG

2
 F P A S S S D I V M T Q S P L S L P V T -

CCTGGAGAGCCGGCCTCCATCTCCTGCAGGTCTAGTCAGAGCATTGTACATAGTAATGGA
 121 -----+-----+-----+-----+-----+ 180
 GGACCTCTCGGCCGGAGGTAGAGGACGTCCAGATCAGTCTCGTAACATGTATCATTACCT

CDR 1

P G E P A S I S C R S S Q S I V H S N G -

KpnI
 |

AACACCTATTTGCAATGGTACCTGCAGAAGCCAGGGCAGTCTCCACAGCTCCTGATCTAT
 181 -----+-----+-----+-----+-----+ 240
 TTGTGGATAAACGTTACCATGGACGTCTTCGGTCCCGTCAGAGGTGTCGAGGACTAGATA

N T Y L Q W Y L Q K P G Q S P Q L L I Y -

AAAGTTTCTAATCGGCTTTATGGGGTCCCTGACAGGTTTCAGTGGCAGTGGATCAGGCACA
 241 -----+-----+-----+-----+-----+ 300
 TTTCAAAGATTAGCCGAAATACCCAGGGACTGTCCAAGTCACCGTCACCTAGTCCGTGT

CDR 2

K V S N R L Y G V P D R F S G S G S G T -

GATTTTACACTGAAAATCAGCAGAGTGGAGGCTGAGGATGTTGGGGTTTATTACTGCTTT
 301 -----+-----+-----+-----+-----+ 360
 CTAAAATGTGACTTTTAGTCGTCTCACCTCCGACTCCTACAACCCCAAATAATGACGAAA

D F T L K I S R V E A E D V G V Y Y C F -

CAAGGTTACATGTTCCGTGGACGTTTCGGCCAAGGGACCAAGGTGGAATCAAACGTGAG
 361 -----+-----+-----+-----+-----+ 420
 GTTCCAAGTGTAAGGCACCTGCAAGCCGGTTCCTGGTTCCACCTTTAGTTTGCACTC

CDR 3

Q G S H V P W T F G Q G T K V E I K

BamHI
 |
 TGGATCCTCTGCG
 421 -----+----- 433
 ACCTAGGAGACGC

FIGURE 21

	17	27	CDR 1
7C10 VH	DVQLQESGPGLVKPSQSLSLTCSVTGYSIT		GGYLWN WIRQ
AN03' CL		S..Y..
Kabat sgI(A)	<u>E</u> <u>S</u> <u>T</u> <u>D</u> ...		S..WN. ...

	CDR 2
7C10 VH	FPGNKLEWMG YISYDGTNNYKPSLKD RISITRDTSKNQFFL
AN03' CLN...N...N...N
Kabat sgI(A)S.STY.N...S <u>Y</u> ..

	84	CDR 3
7C10 VH	KLNSVTNEDTATYYCAR	YGRV-FFDY WGQGTTLTVSS
AN03' CL <u>T</u>	E.YGY
Kabat sgI(A)	<u>Q</u> <u>T</u>	G.YGYG <u>V</u>

FIGURE 22

	Rch 1	30	CDR 1	Rch 2
7C10 VH mouse	DVQLQESGPGLVKPSQSLSLTCSVTGYSIT		GGYLWN	WIRQ
human Kabat sgII	Q.....T.....T.S. <u>G</u> . <u>V</u> S		SYWS
human VH FUR1'CL	Q.....ET.....T.S....S		S..Y.S
human Germline	Q.....ET.....T.S....S		S..Y.S

	Rch 2	48	CDR 2	67	71	Rch 3
7C10 VH mouse	FPGNKLEWMG		YISYDGTNNYKPSLKD			RISITRDTSKNQFFL
human Kabat sgII	P..KG...I.		R.Y.S.STX.N....S			.VT.SV.....S.
human VH FUR1'CL	P..KG...I.		SMFHS.SSY.N....S			.VT.SV.....S.
human Germ-line	P..KG...I.		S.YHS.STY.N....S			.VT.SV.....S.

	Rch 3	CDR 3	Rch 4
7C10 VH mouse	KLNSVTNEDTATYYCAR	YGRVFFDY	WGQGTTLTVSS
human Kabat sgII	..S...AA...V.....	ELPGGYDVLV....
human VH FUR1'CL	Q.R...AA...V.....	GRYCSSTSCNWFDPLV....
human Germline	..S...AA...V.....		

FIGURE 23

		30	CDR 1	48
7C10 VH mouse	DVQLQESGPGLVKPSQSLTCSVTGYSIT	<u>GGYLWN</u>	WIRQFPGNKLEW	<u>MG</u>
human germline	Q.....ET.....T.S....	<u>S</u> <u>S</u> ..Y.GP..KG...	<u>I</u> ..
VH Humanized 1	Q.....ET.....T.S....	P..KG....	
VH Humanized 2	Q.....ET.....T.S....	P..KG...	<u>I</u> ..
VH Humanized 3	Q.....ET.....T.S....	<u>S</u>P..KG...	<u>I</u> ..

	CDR 2	67	71
7C10 VH mouse	<u>YISYDGTNNYKPSLKD</u>	RISITR	DTSKNQFFLKLNSVTNEDTATYYCAR
human germline	<u>S.FHS.SSY.N</u>S	<u>VT</u> . <u>SV</u>S	S...AA...V.....
VH Humanized 1		.T.S.....S	S...AA...V.....
VH Humanized 2		<u>VT</u> .S.....S	S...AA...V.....
VH Humanized 3		<u>VT</u> . <u>SV</u>S	S...AA...V.....

	CDR 3
7C10 VH mouse	<u>YGRVFFDY</u> WGQGTTLTVSS
human germline	
VH Humanized 1LV....
VH Humanized 2LV....
VH Humanized 3LV....

FIGURE 24

MluI

```

      |
GTCAGAACGCGTGCCGCCACCATGAAAGTGTTGAGTCTGTTGTACCTCTTGACAGCCATT
1  -----+-----+-----+-----+-----+-----+ 60
CAGTCTTGCGCACGGCGGTGGTACTTTTCAAACTCAGACAACATGGAGAACTGTCGGTAA

      M K V L S L L Y L L T A I -
      Leader peptide
CCTGGTATCCTGTCTCAGGTGCAGCTTCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCG
61 -----+-----+-----+-----+-----+-----+ 120
GGACCATAGGACAGAGTCCACGTCTGAAGTCCTCAGCCCGGGTCCTGACCACTTCGGAAGC

P G I L S Q V Q L Q E S G P G L V K P S -
GAGACCCTGTCCCTCACCTGCACTGTCTCTGGTTACTCCATCACCGGTGGTTATTTATGG
121 -----+-----+-----+-----+-----+-----+ 180
CTCTGGGACAGGGAGTGGACGTGACAGAGACCAATGAGGTAGTGGCCACCAATAAATACC

      30          CDR 1
E T L S L T C T V S G Y S I T G G Y L W -
AACTGGATACGGCAGCCCCCAGGGAAGGGACTGGAGTGGATGGGGTATATCAGCTACGAC
181 -----+-----+-----+-----+-----+-----+ 240
TTGACCTATGCCGTCGGGGGTCCCTTCCCTGACCTCACCTACCCCATATAGTCGATGCTG

      48
N W I R Q P P G K G L E W M G Y I S Y D -
      KpnI
      |
GGTACCAATAACTACAAACCCTCCCTCAAGGATCGAATCACCATATCACGTGACACGTCC
241 -----+-----+-----+-----+-----+-----+ 300
CCATGGTTATTGATGTTTGGGAGGGAGTTCCTAGCTTAGTGGTATAGTGCACCTGTGCAGG

      CDR 2          67          71
G T N N Y K P S L K D R I T I S R D T S -
AAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCTGCGGACACTGCAGTGTATTAC
301 -----+-----+-----+-----+-----+-----+ 360
TTCTTGGTCAAGAGGGACTTCGACTCGAGACACTGGCGACGCCTGTGACGTCACATAATG

K N Q F S L K L S S V T A A D T A V Y Y -
TGTGCGAGATACGGTAGGGTCTTCTTTGACTACTGGGGCCAGGGAACCCCTGGTCACCGTC
361 -----+-----+-----+-----+-----+-----+ 420
ACACGCTCTATGCCATCCCAGAAGAACTGATGACCCCGGTCCCTTGGGACCAGTGGCAG

      CDR 3
C A R Y G R V F F D Y W G Q G T L V T V -

      BamHI
      |
TCCTCAGGTGAGTGGATCCTCTGCG
421 -----+-----+-----+-----+ 445
AGGAGTCCACTCACCTAGGAGACGC

S S -
  
```

FIGURE 25

MluI
 |
 GTCAGAACGCGTGCCGCCACCATGAAAGTGTTGAGTCTGTTGTACCTCTTGACAGCCATT
 1 -----+-----+-----+-----+-----+-----+ 60
 CAGTCTTGCGCACGGCGGTGGTACTTTCACAACCTCAGACAACATGGAGAACTGTCGGTAA

M K V L S L L Y L L T A I -
 Leader peptide

CCTGGTATCCTGTCTCAGGTGCAGCTTCAGGAGTCGGGCCAGGACTGGTGAAGCCTTCG
 61 -----+-----+-----+-----+-----+-----+ 120
 GGACCATAGGACAGAGTCCACGTCTGAAGTCCTCAGCCCCGGGTCTGACCACTTCGGAAGC

P G I L S Q V Q L Q E S G P G L V K P S -

GAGACCCTGTCCCTCACCTGCAGTGTCTCTGGTTACTCCATCACCGGTGGTTATTTATGG
 121 -----+-----+-----+-----+-----+-----+ 180
 CTCTGGGACAGGGAGTGGACGTGACAGAGACCAATGAGGTAGTCGCCACCAATAAATACC

30 CDR 1
 E T L S L T C T V S G Y S I T G G Y L W -

AACTGGATACGGCAGCCCCCAGGGAAGGGACTGGAGTGGATCGGGTATATCAGCTACGAC
 181 -----+-----+-----+-----+-----+-----+ 240
 TTGACCTATGCCGTGCGGGGTCCCTTCCCTGACCTACCTAGCCCATATAGTCGATGCTG

48
 N W I R Q P P G K G L E W I G Y I S Y D -

KpnI
 |
 GGTACCAATAACTACAAACCCTCCCTCAAGGATCGAGTCACCATATCACGTGACACGTCC
 241 -----+-----+-----+-----+-----+-----+ 300
 CCATGGTTATTGATGTTTGGGAGGGAGTTCCTAGCTCAGTGGTATAGTGCACTGTGCAGG

CDR 2 67 71
 G T N N Y K P S L K D R V T I S R D T S -

AAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCTGCGGACACTGCAGTGTATTAC
 301 -----+-----+-----+-----+-----+-----+ 360
 TTCTTGGTCAAGAGGGACTTCGACTCGAGACACTGGCGACGCCTGTGACGTACATAATG

K N Q F S L K L S S V T A A D T A V Y Y -

TGTGCGAGATACGGTAGGGTCTTCTTTGACTACTGGGGCCAGGGAACCCTGGTACCGTC
 361 -----+-----+-----+-----+-----+-----+ 420
 ACACGCTCTATGCCATCCCAGAAGAACTGATGACCCCGGTCCCTTGGGACCACTGGCAG

CDR 3
 C A R Y G R V F F D Y W G Q G T L V T V -

BamHI
 |
 TCCTCAGGTGAGTGGATCCTCTGCG
 421 -----+-----+-----+-----+ 445
 AGGAGTCCACTCACCTAGGAGACGC

S S -

FIGURE 26

MluI
 |
 GTCAGAACGCGTGCCGCCACCATGAAAGTGTTGAGTCTGTTGTACCTCTTGACAGCCATT
 1 -----+-----+-----+-----+-----+-----+-----+ 60
 CAGTCTTGCGCACGGCGGTGGTACTTTTCACTCAGACAACATGGAGAACTGTCGGTAA

M K V L S L L Y L L T A I -
 Leader peptide
 CCTGGTATCCTGTCTCAGGTGCAGCTTCAGGAGTCGGGCCCAGGACTGGTGAAGCCTTCG
 61 -----+-----+-----+-----+-----+-----+ 120
 GGACCATAGGACAGAGTCCACGTGCAAGTCCTCAGCCCCGGTCTGACCACTTCGGAAGC

P G I L S Q V Q L Q E S G P G L V K P S -
 GAGACCCTGTCCCTCACCTGCACTGTCTCTGGTTACTCCATCAGCGGTGGTTATTTATGG
 121 -----+-----+-----+-----+-----+-----+ 180
 CTCTGGGACAGGGAGTGGACGTGACAGAGACCAATGAGGTAGTCGCCACCAATAAATACC

30 CDR 1
 E T L S L T C T V S G Y S I S G G Y L W -
 AACTGGATACGGCAGCCCCCAGGGAAGGGACTGGAGTGGATCGGGTATATCAGCTACGAC
 181 -----+-----+-----+-----+-----+-----+ 240
 TTGACCTATGCCGTGCGGGGTCCCTTCCCTGACCTACCTAGCCCATATAGTCGATGCTG

48
N W I R Q P P G K G L E W I G Y I S Y D -
 KpnI
 |
 GGTACCAATAACTACAAACCCTCCCTCAAGGATCGAGTCACCATATCAGTGGACACGTCC
 241 -----+-----+-----+-----+-----+-----+ 300
 CCATGGTTATTGATGTTTGGGAGGGAGTTCCTAGCTCAGTGGTATAGTCACCTGTGCAGG

CDR 2 67 71
 G T N N Y K P S L K D R V T I S V D T S -
 AAGAACCAGTTCTCCCTGAAGCTGAGCTCTGTGACCGCTGCGGACACTGCAGTGTATTAC
 301 -----+-----+-----+-----+-----+-----+ 360
 TTCTTGGTCAAGAGGGACTTCGACTCGAGACACTGGCGACGCCTGTGACGTCACATAATG

K N Q F S L K L S S V T A A D T A V Y Y -
 TGTGCGAGATACGGTAGGGTCTTCTTTGACTACTGGGGCCAGGGAACCCTGGTCACCGTC
 361 -----+-----+-----+-----+-----+-----+ 420
 ACACGCTCTATGCCATCCAGAAGAACTGATGACCCCGGTCCCTTGGGACCACTGGCAG

CDR 3
 C A R Y G R V F F D Y W G Q G T L V T V -
 BamHI
 |
 TCCTCAGGTGAGTGGATCCTCTGCG
 421 -----+-----+-----+-----+-----+ 445
 AGGAGTCCACTCACCTAGGAGACGC

S S

FIGURE 27

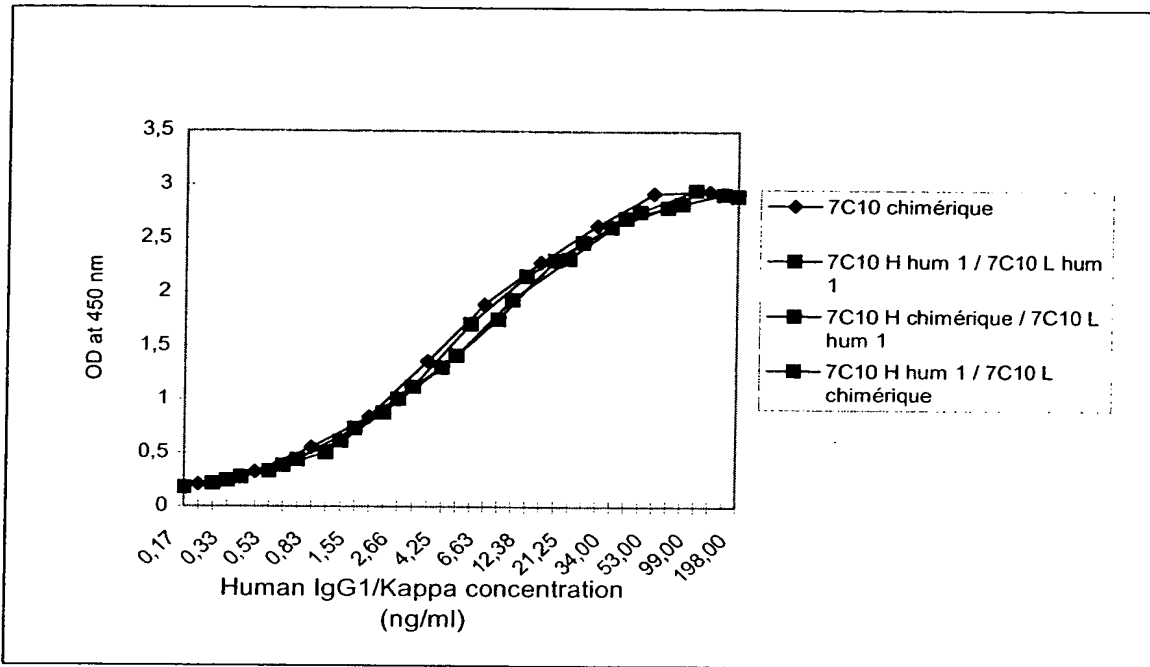


FIGURE 28

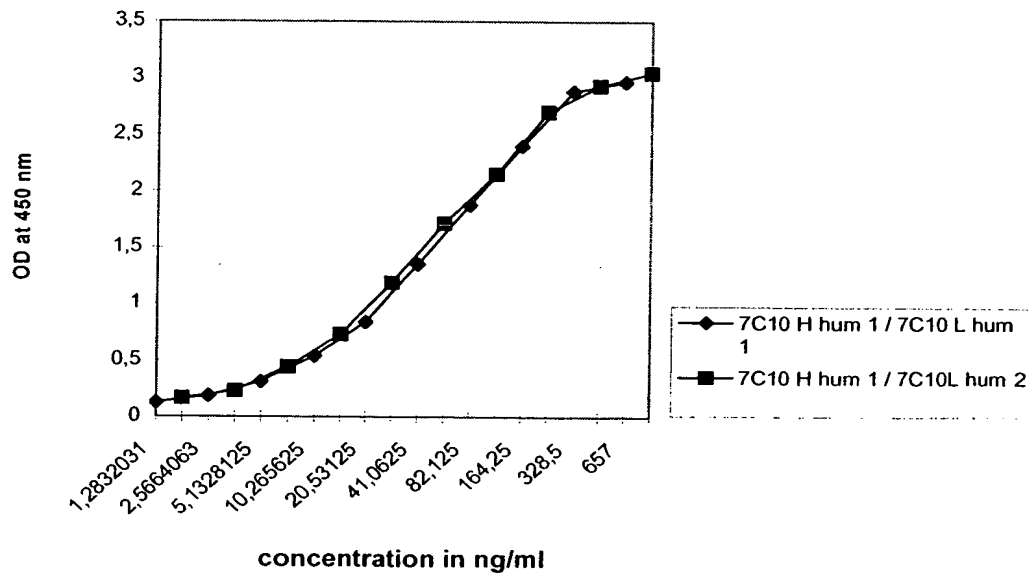


FIGURE 29

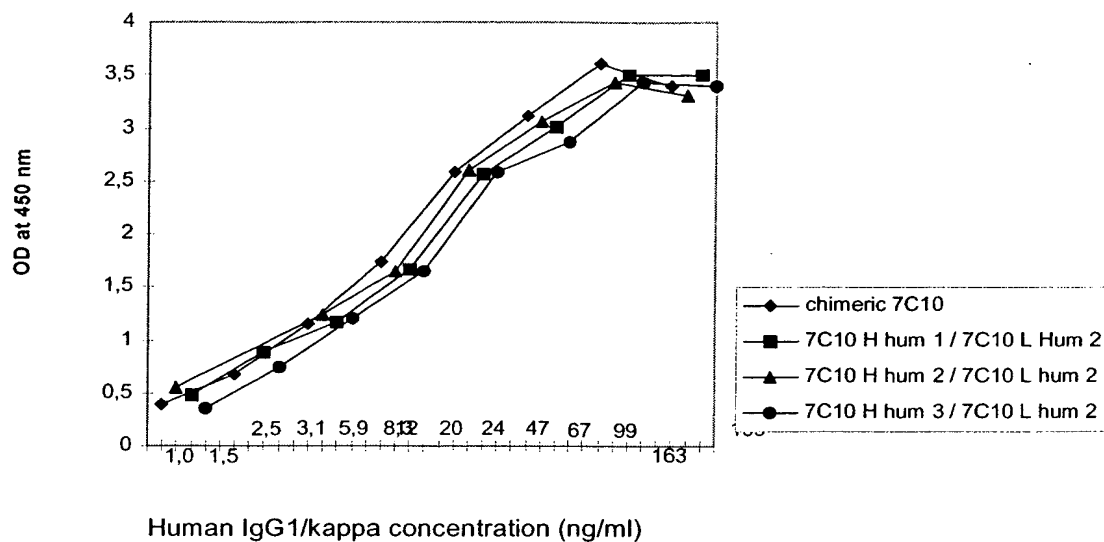


FIGURE 30

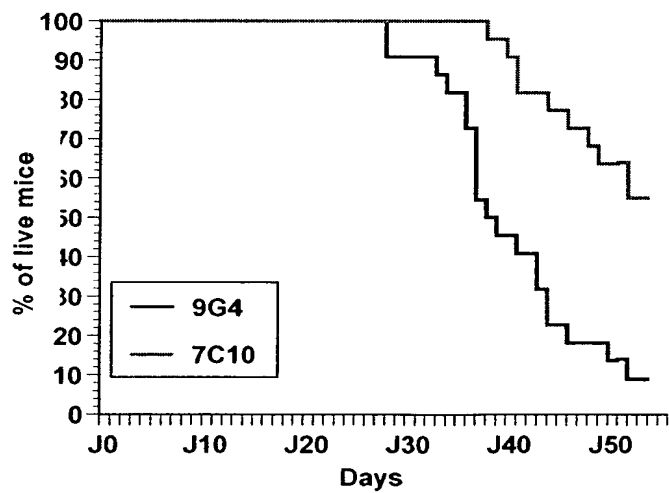


FIGURE 31

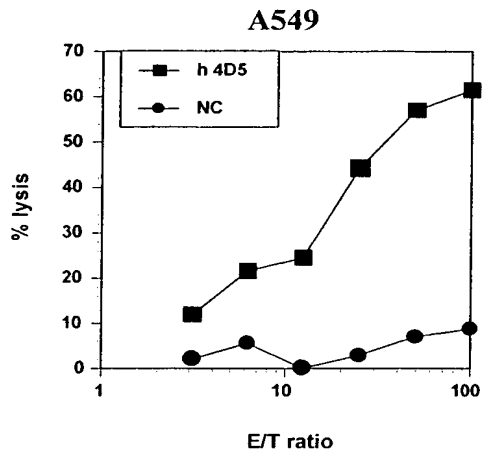


FIGURE 32A

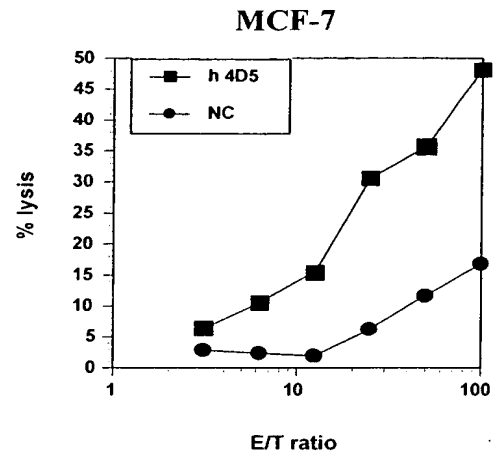


FIGURE 32B

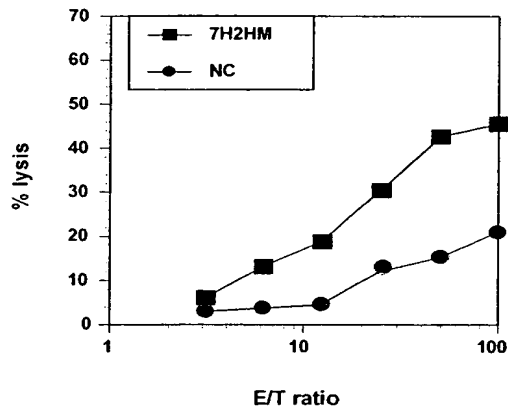


FIGURE 32C

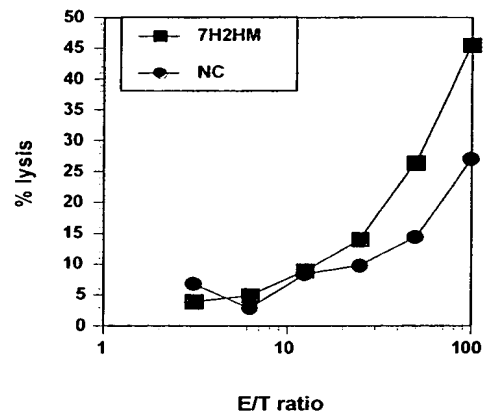


FIGURE 32D

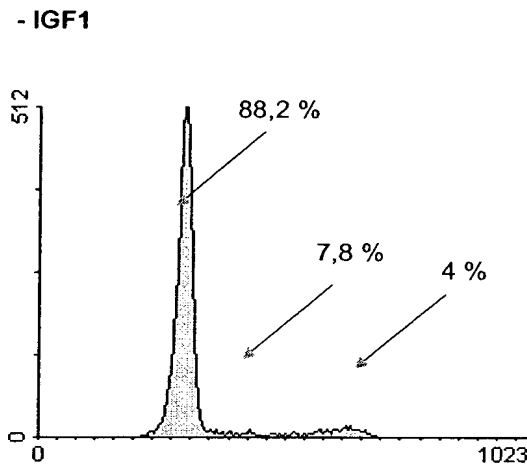


FIGURE 33A

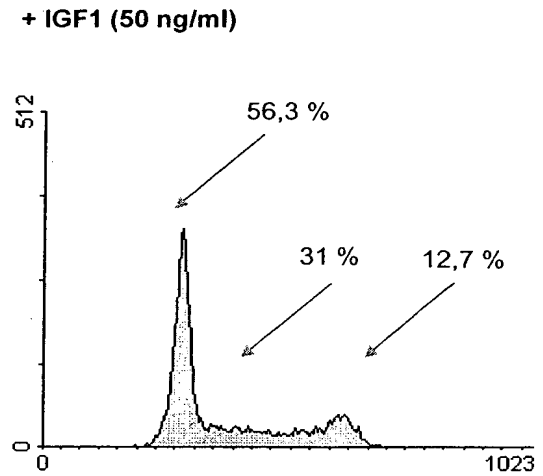


FIGURE 33B

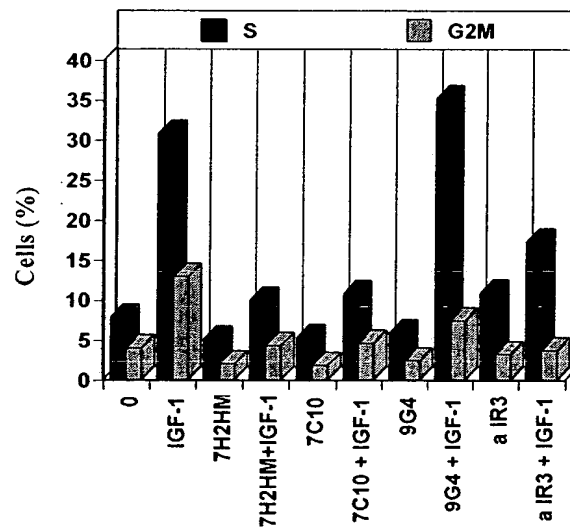


FIGURE 33C

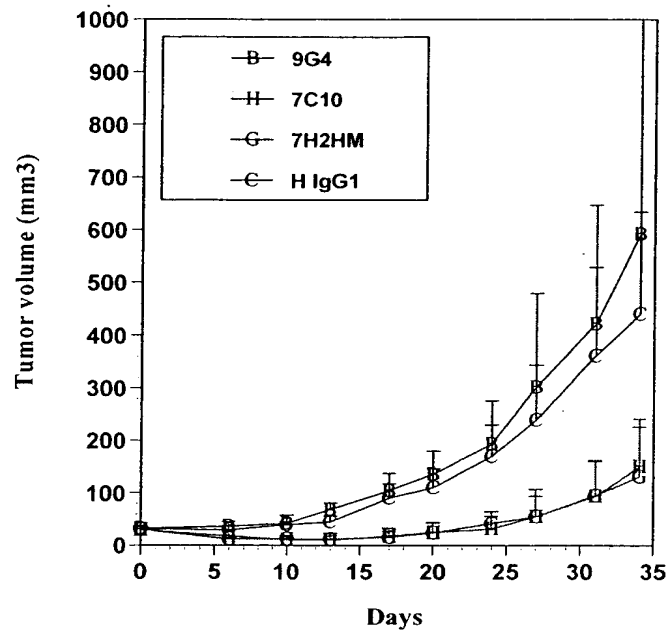


FIGURE 34A

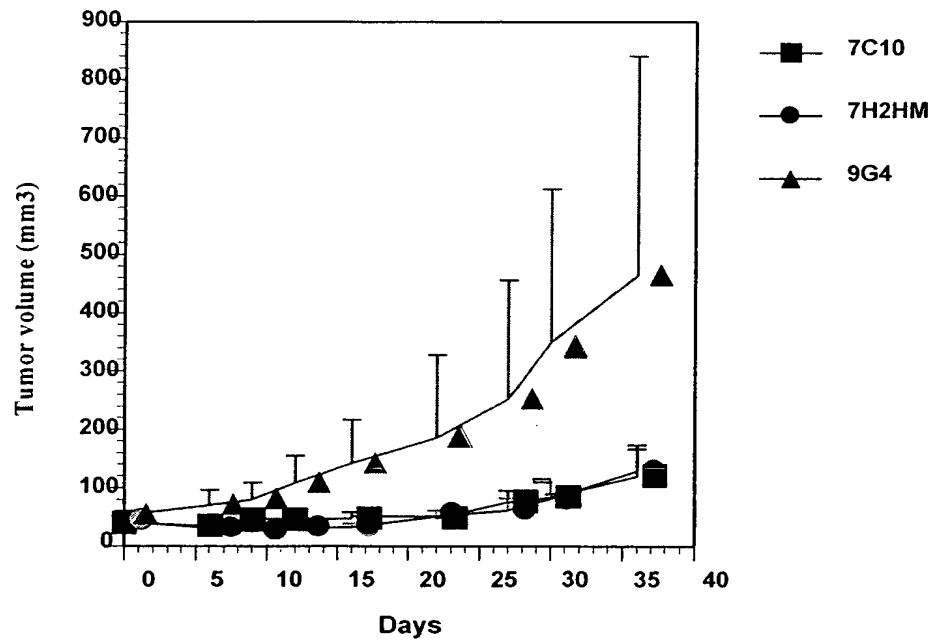


FIGURE 34B

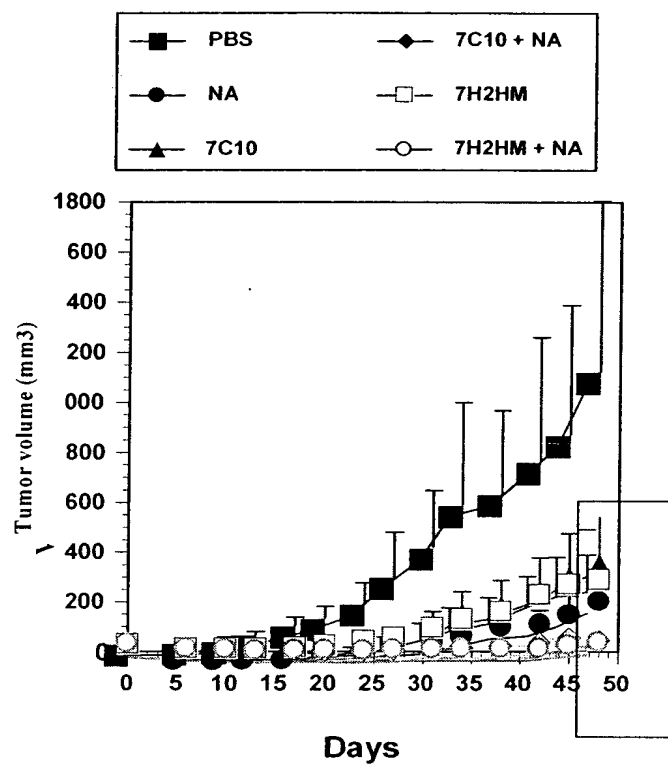


FIGURE 35A

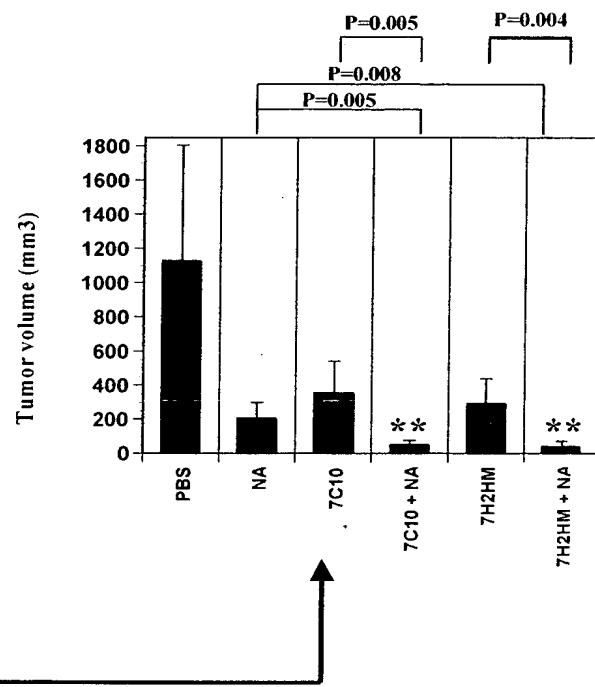


FIGURE 35B

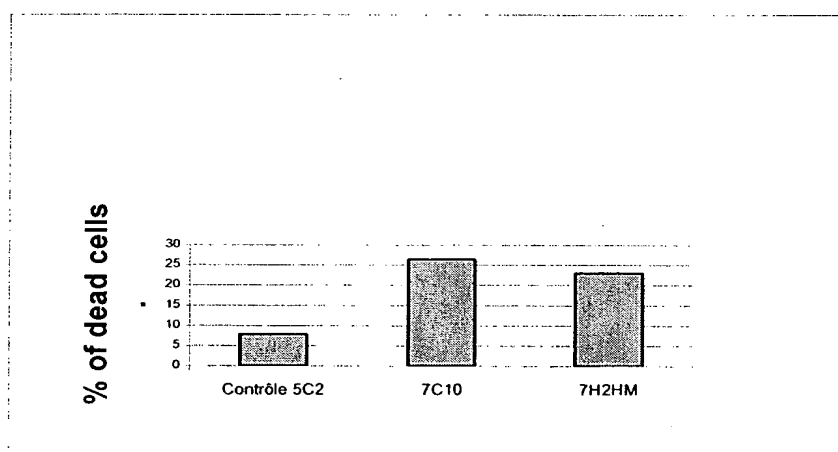


FIGURE 36

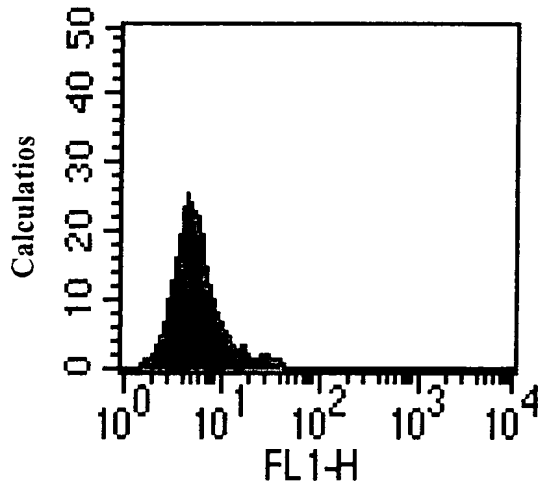


FIGURE 37A

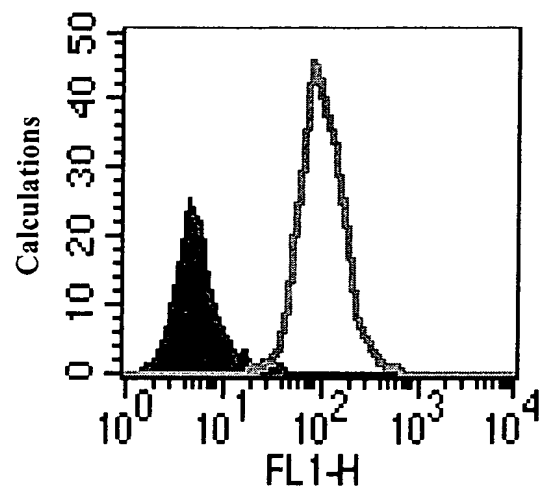


FIGURE 37B

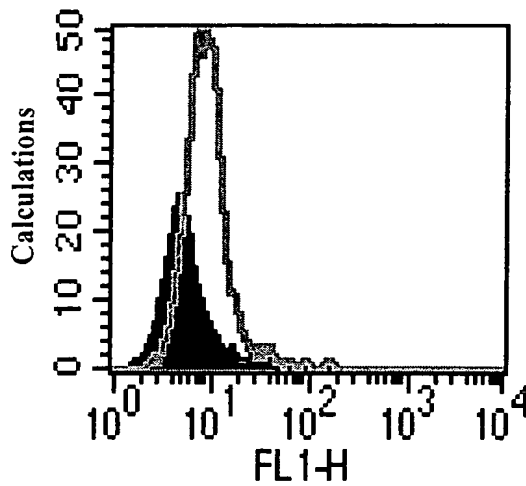


FIGURE 37C

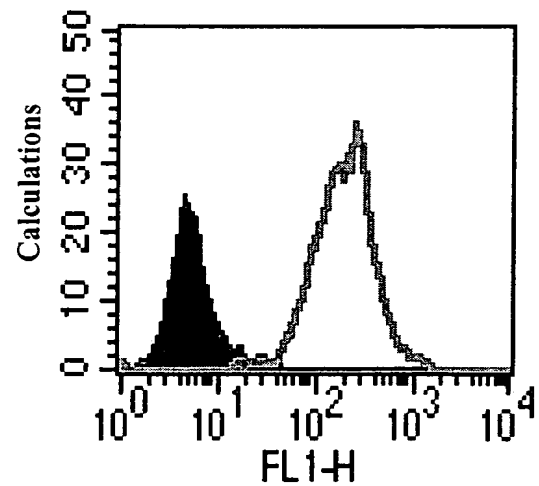


FIGURE 37D

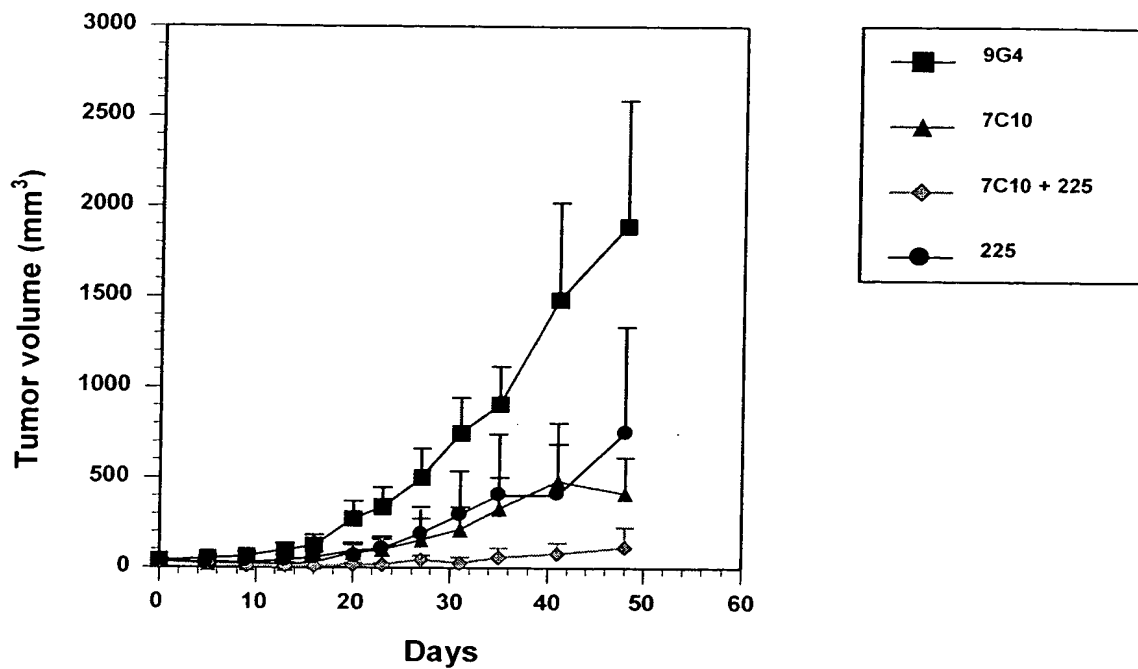


FIGURE 38

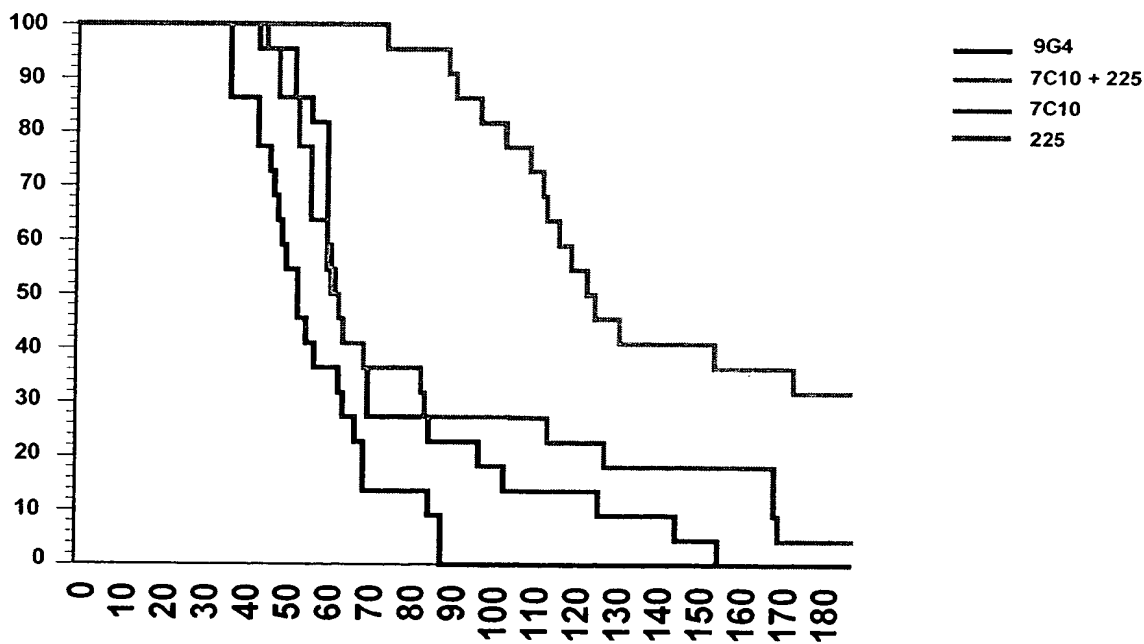


FIGURE 39

FIGURE 40A

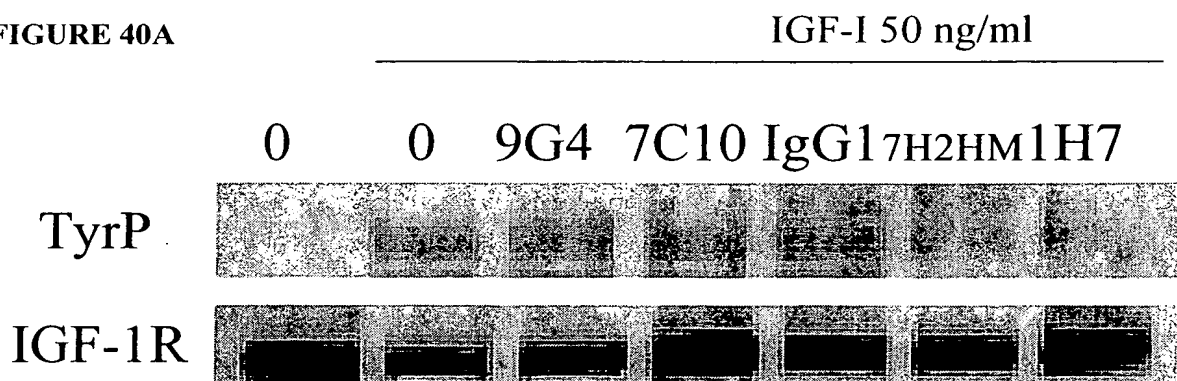


FIGURE 40B

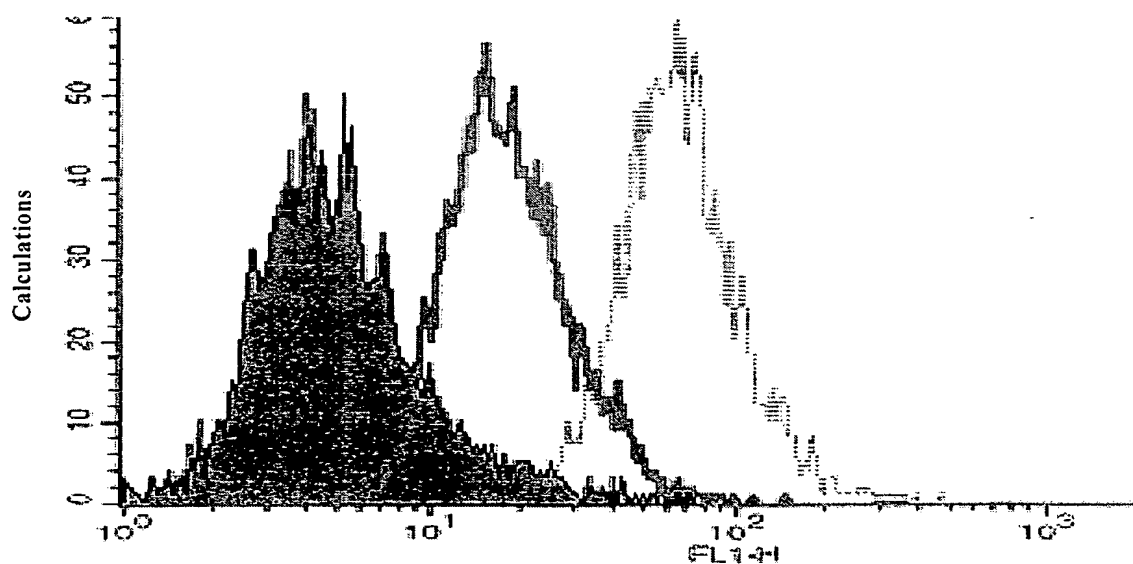
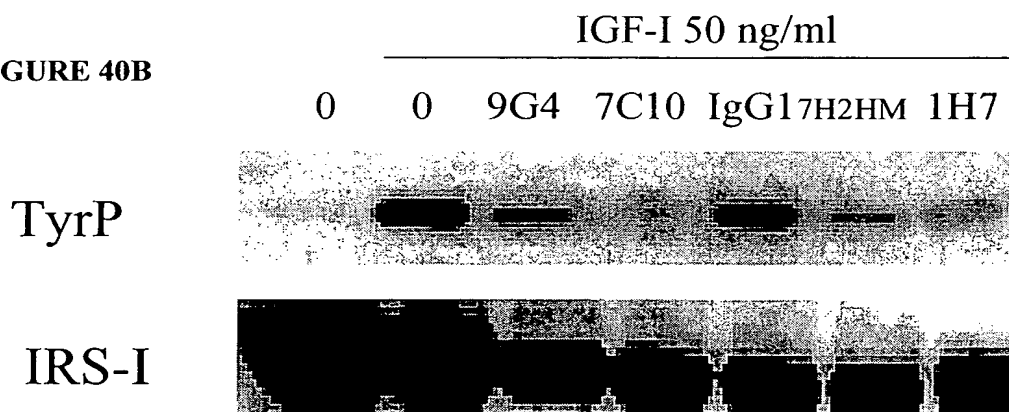


FIGURE 41

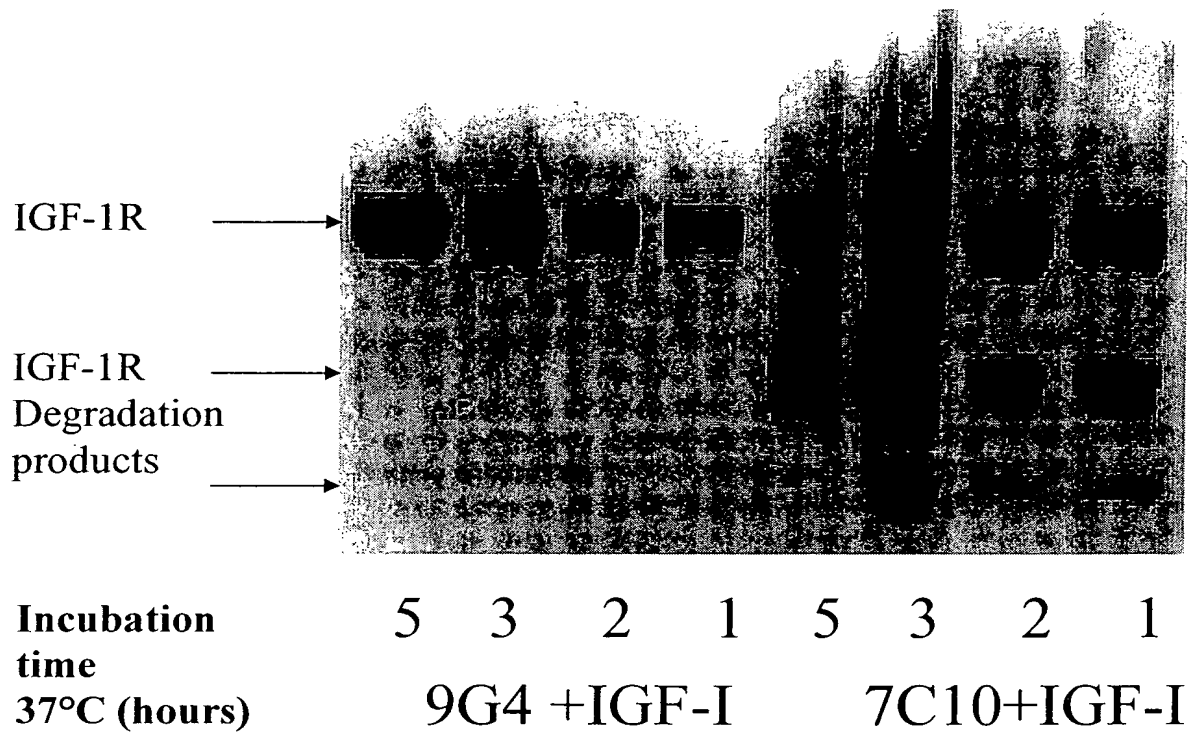


FIGURE 42A

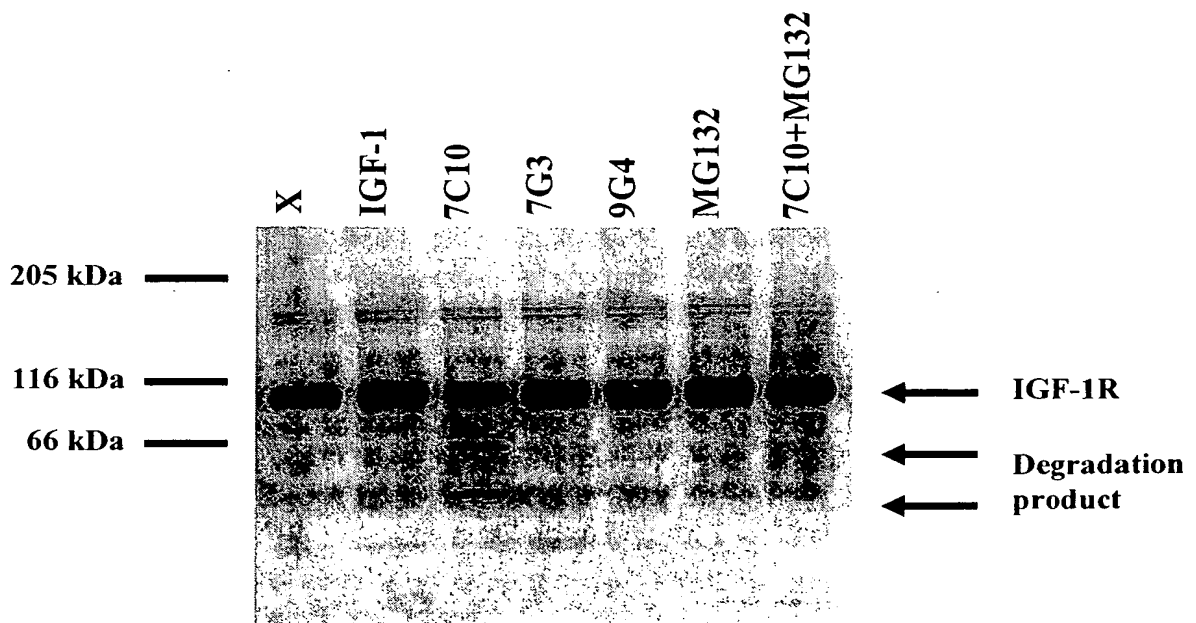


FIGURE 42B

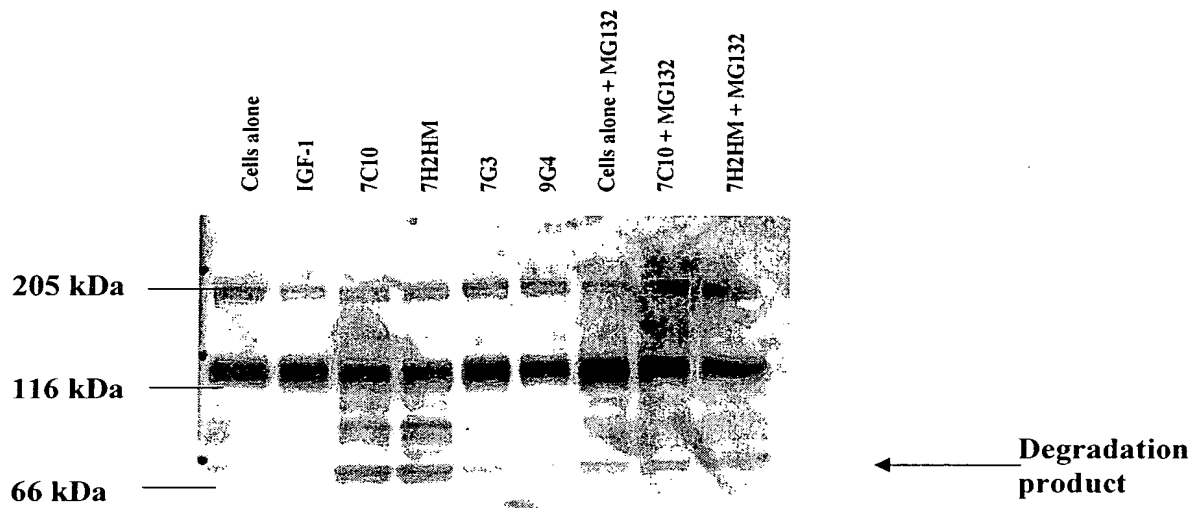


FIGURE 42C

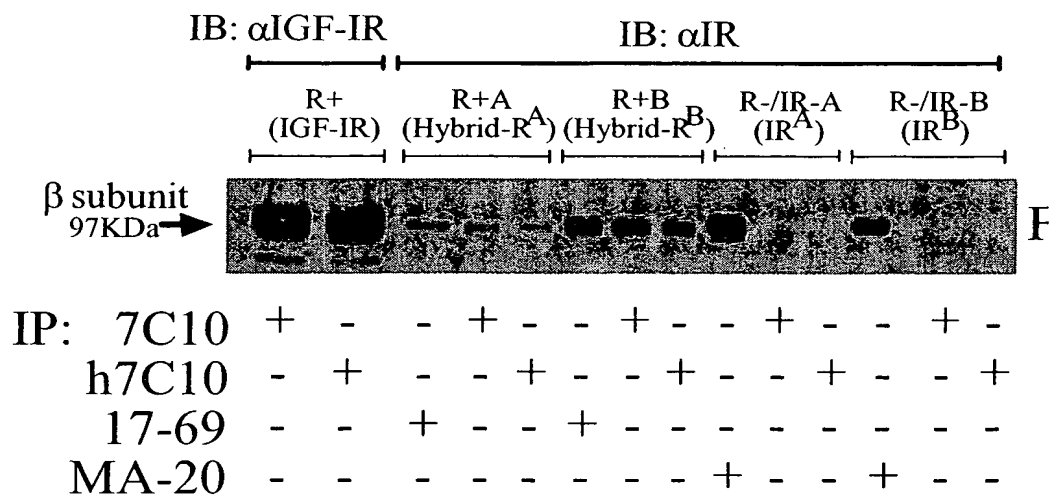


FIGURE 43A

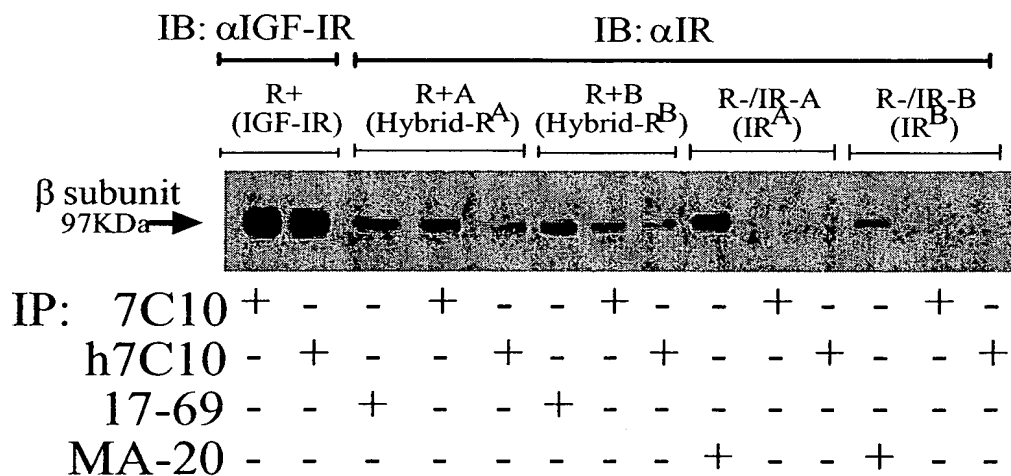


FIGURE 43B

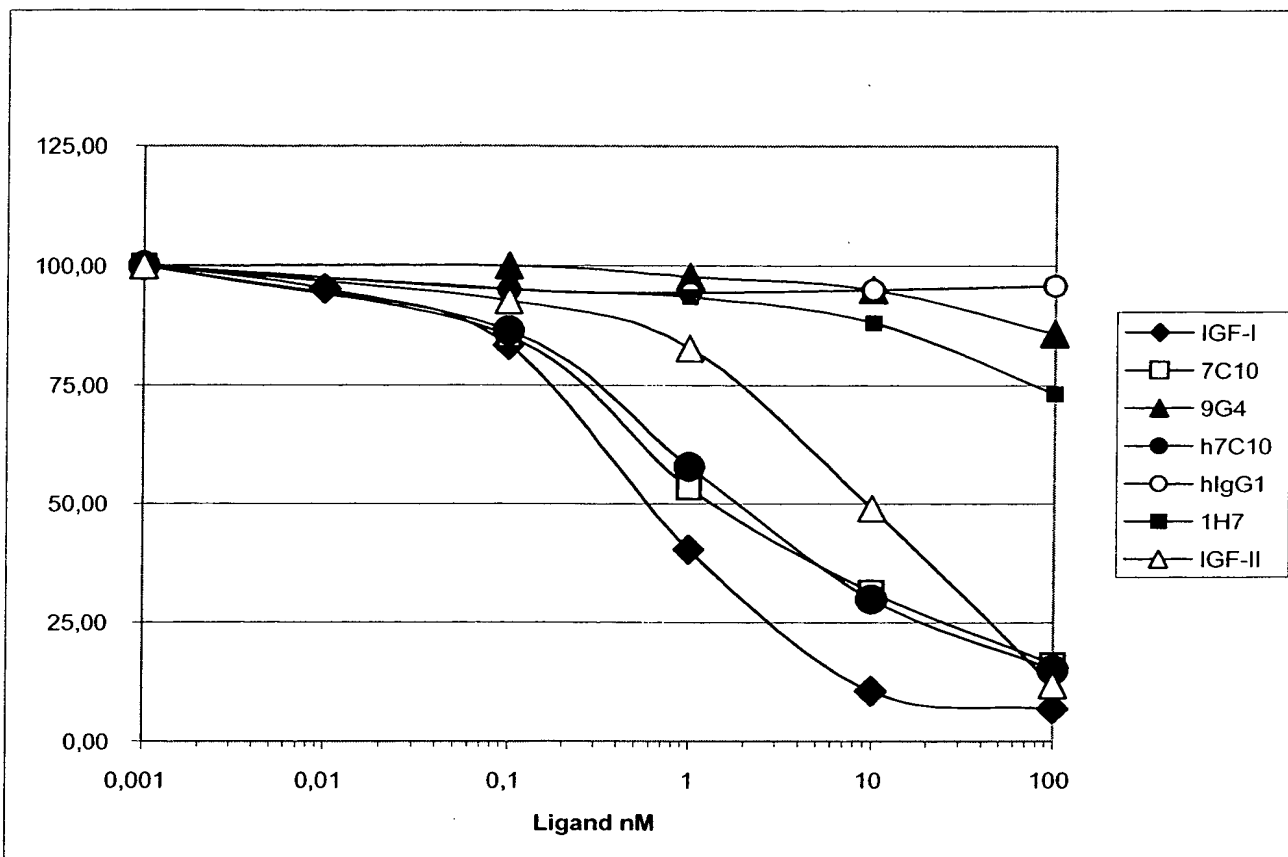


FIGURE 44

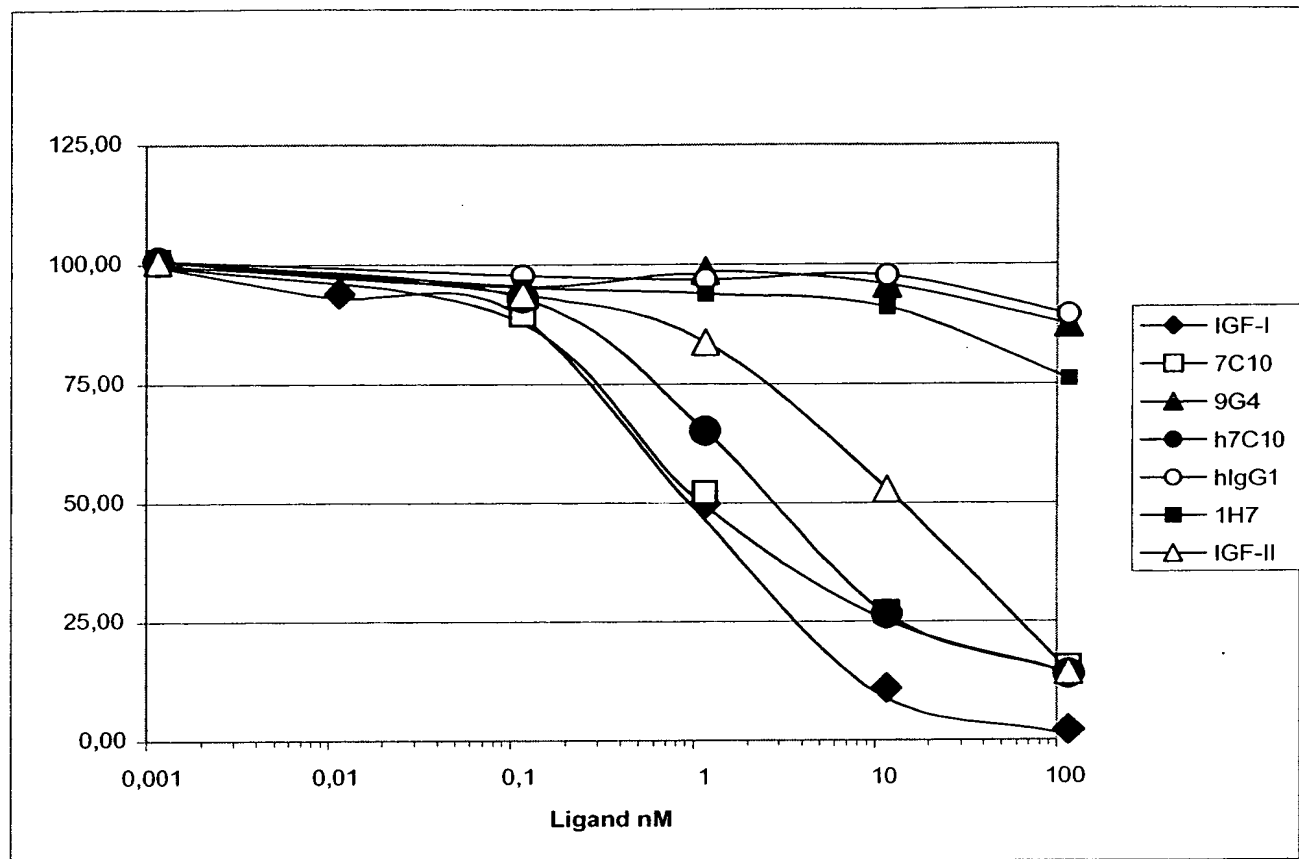


FIGURE 45

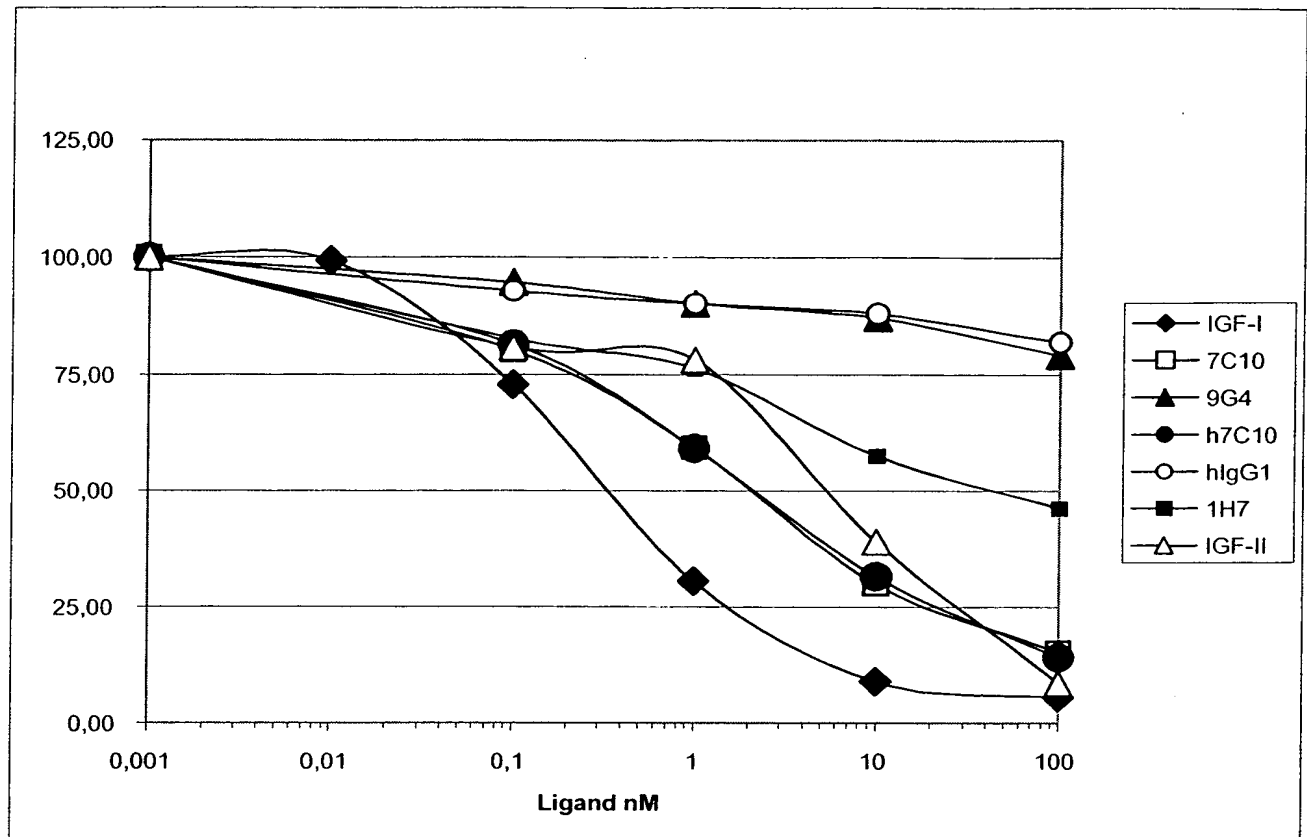


FIGURE 46

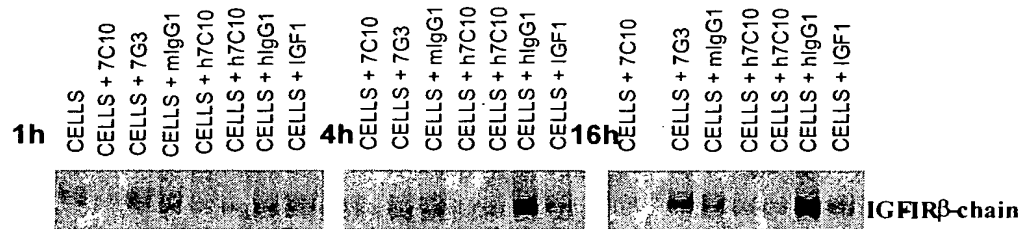


FIGURE 47A

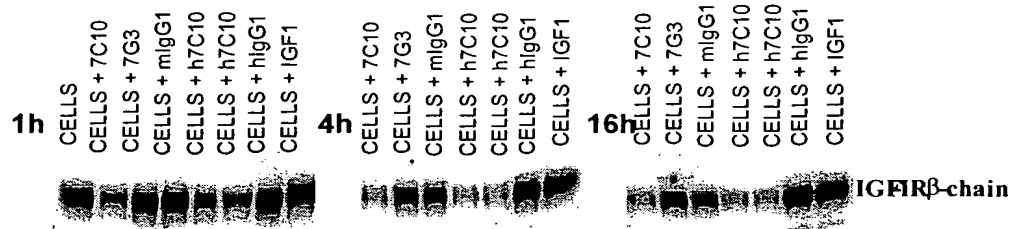


FIGURE 47B

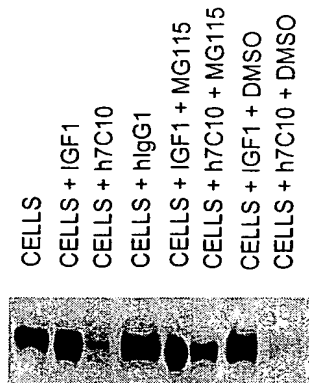


FIGURE 48

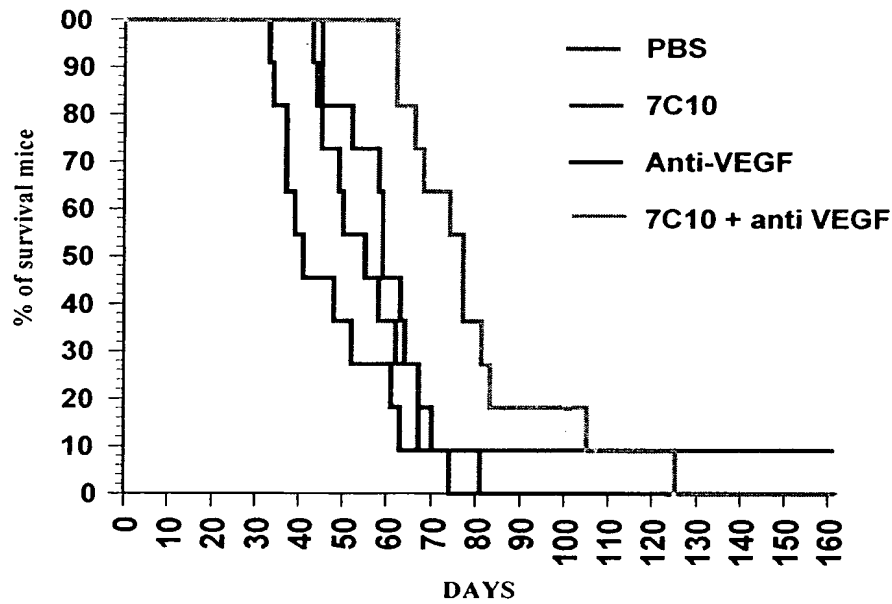


FIGURE 49

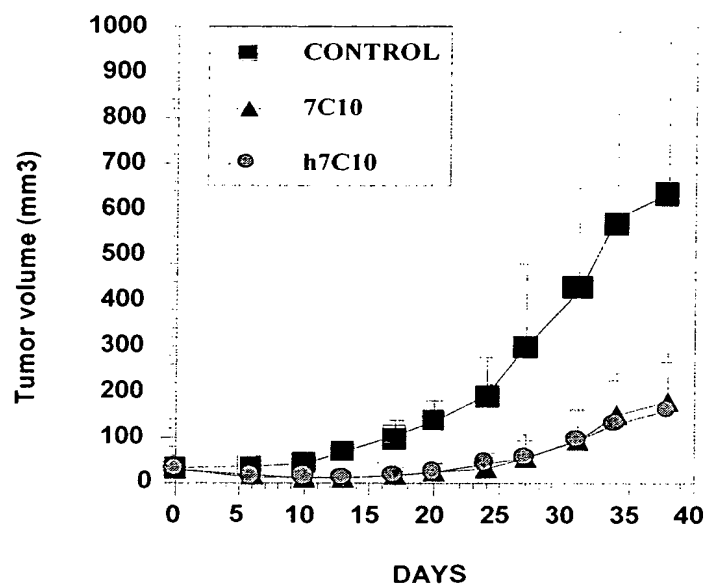


FIGURE 50

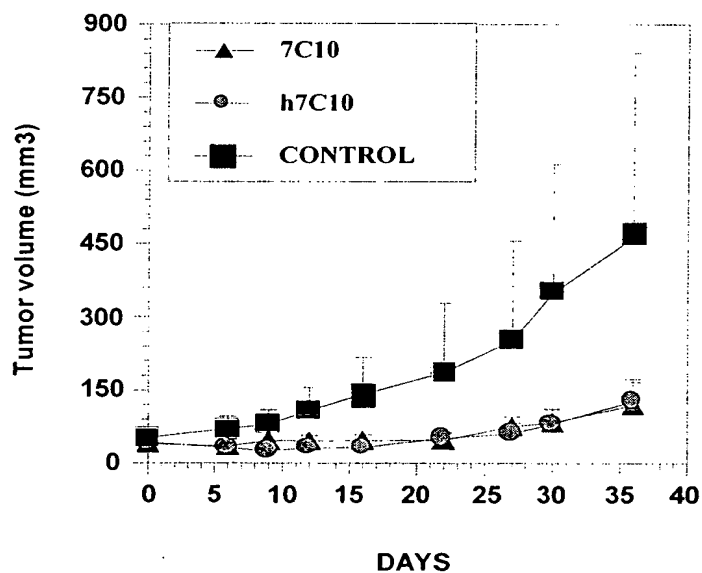


FIGURE 51

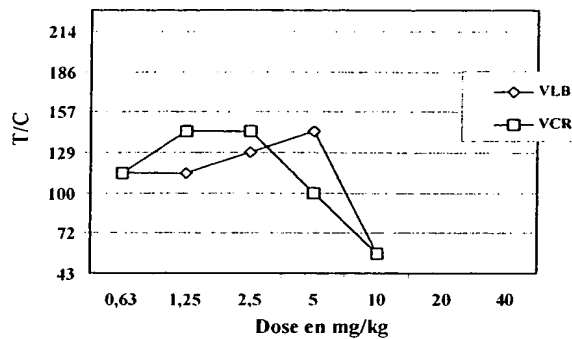


FIGURE 52

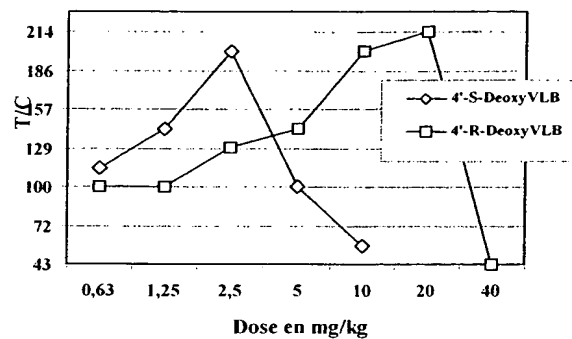


FIGURE 53

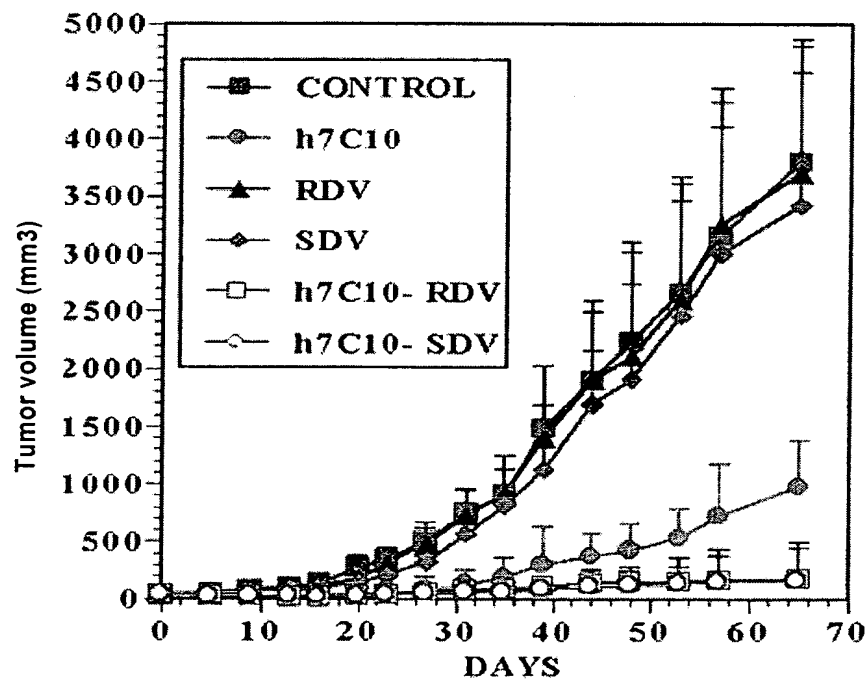


FIGURE 54

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